**Helping people cope with temptations to smoke to reduce relapse: A curtailed randomised controlled trial (Relapse Prevention Study)**

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At the time of the study, Ron Borland and Lin Li worked for Cancer Council Victoria which owns the intellectual property for the S3P that was adapted in this trial. Ron Borland co-developed the S3P intervention as part of his former employment at Cancer Council Victoria. He has no financial interest in the tool, but continues to research and explore improvements to it. James Balmford co-developed the S3P intervention with Ron Borland as part of his former employment at Cancer Council Victoria. At the time of the study he was employed by the University of Freiburg, Germany and had no financial interest in the tool. In March 2020, while this report was being revised he died suddently after a short illness. He made a large contribution to the study and is greatly missed.

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All other co-applicants have nothing to declare.

**Key words:** relapse prevention, smoking, electronic cigarette, nicotine products, online intervention

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**Abstract**

**Background:** Relapse remains an unresolved issue in smoking cessation. Extended stop-smoking medication use can help, but uptake is low and several behavioural relapse prevention interventions were found ineffective. However, opportunistic ‘emergency’ use of fast acting nicotine replacement treatment (NRT) or electronic cigarettes may be more attractive and effective and an online behavioural Structured Planning and Prompting Protocol (S3P) has shown promise. The present trial aimed to evaluate the effectiveness of these two interventions.

**Design:** RCT

**Setting/participants:** Recent (four week) ex-smokers (234 rather than the planned 1400) recruited from English stop smoking services and Australian quitlines. Participants in Australia were also later recruited via social media and St Vincent’s Hospital, Melbourne from one week quit.

**Interventions:** Participants were randomised in permuted blocks of random sizes to1) Oral NRT/e-cigarette to use if at risk of relapse, plus static text messages (N=60), 2) S3P and interactive text messaging (N=57), 3) Oral NRT/e-cigarette plus S3P with interactive text messaging (N=58), 4) usual care plus static text messages (N=59).

**Outcome measures:** Due to delays in study set-up and recruitment issues, the study was curtailed, and the primary outcome was revised. The original objective was whether the two interventions, together or separately, reduced relapse rates at 12 months compared to usual care. The revised primary objective was whether number of interventions received (none, one or two) affects relapse rate at six months (not biochemically validated due to study curtailment). Relapse was defined as smoking on at least seven consecutive days, or any smoking in the last month at final follow up for both the original and curtailed outcomes. Participants with missing outcome data were included as smokers. Secondary outcomes included sustained abstinence (≤5 cigarettes smoked over the six months), nicotine product preferences (e.g. e-cigarette or NRT) and S3P coping strategies used. Two sub studies assessed reactions to interventions quantitatively and qualitatively. The trial statistician remained blinded until analysis was complete.

**Results:** The six-month relapse rates were 60.0%, 43.5% and 49.2% in the usual care, one intervention, and both intervention arms, respectively (p=0.11). Sustained abstinence rates were 41.7%, 54.8% and 50.9%, respectively (p=0.17). E-cigarette was chosen more frequently than NRT in Australia (71.1% versus 29.0%, p=.001), but not in England (54.0% versus 46.0%, p=0.57). Of participants allocated to nicotine products, 23.1% were using daily at six months. The online intervention received positive ratings from 63% of participants at six months, but the majority of participants (72%) only completed one assessment. Coping strategies taught in S3P were used with similar frequency in all study arms, suggesting these are strategies people had already acquired. Only one participant used the interactive texting and interactive and static messages received virtually identical ratings.

**Limitations:** The inability to recruit sufficient participants resulted in lack of power to detect clinically relevant differences. Self-reported abstinence was not biochemically validated in the curtailed trial, and the EMA sub study was perceived by some as an intervention.

**Conclusions:** Recruiting recent ex-smokers into an interventional study proved problematic. Both interventions were well received and safe. Combining the interventions did not surpass the effects of each intervention alone. There was a trend in favour of single interventions reducing relapse, but it did not reach significance and there are reasons to interpret the trend with caution.

**Future work:** Further studies of both interventions are warranted, using simpler study designs.

**Funding:** National Institute for Health Research (NIHR) Health Technology Assessment, UK and National Health and Medical Research Council (NHMRC APP1095880), Australia. Public Health England (PHE) provided the funds to purchase the nicotine products in England.

**Trial registration:** This trial was registered on the ISRCTN registry (ISRCTN11111428).

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# List of abbreviations

AE: Adverse Event

AR: Adverse Reaction

CI: Chief Investigator

CRF: Case Report Form

CTU: Clinical Trials Unit

DMEC: Data Monitoring and Ethics Committee

EC: Electronic cigarette

EMA: Ecological Momentary Assessment

GCP: Good Clinical Practice

JRMO: Joint Research Management Office

NIC: Nicotine product study arm

NRT Nicotine Replacement Treatment

QD: Quit Date

RCT: Randomised Controlled Trial

REC: Research Ethics Committee

RP: Relapse Prevention

SAE: Serious Adverse Event

SOP: Standard Operating Procedure

SSS: Stop Smoking Service

S3P: Structured Planning and Prompting Protocol

TMG: Trial Management Group

TSC: Trial Steering Committee

UC: Usual Care

Plain English Summary

Stop smoking services help people to stop smoking over a short period of time. However, nearly three-quarters of quitters usually return to smoking (relapse) within a year. Effective relapse prevention strategies are needed.

Traditional behavioural relapse prevention strategies (e.g. teaching techniques to resist having a cigarette) have not proved effective. However, an Australian trial showed that an online programme guiding smokers in stopping smoking and staying quit reduced relapse between one week and six months.

Long-term use of stop smoking medications (e.g. nicotine replacement treatment) can also help, but most successful quitters do not continue to use them. Nicotine mouth spray, lozenges or e-cigarettes that can quickly help relieve urges to smoke and that ex-smokers can use ‘in emergencies’ could be a more attractive option.

We planned to test these two interventions, on their own and together, in 1400 four-week quitters recruited from English stop smoking services and Australian quitlines, and compare them to usual care (typically comprising access to stop smoking medications used during the quit attempt for up to three months).

Due to delays in study set-up and difficulties in recruiting, the study only recruited 234 participants (131 in Australia and 103 in England).

We studied participants’ reactions to the two interventions and to their combination, and how effective the interventions were.

Both interventions were rated positively by most participants. Among the participants in Australia, e-cigarettes were more popular than medical nicotine products but in England, both products were equally popular. Participants in the online intervention group appreciated the advice on coping strategies, but they rarely completed repeat assessments, and participants who were not in this group also used the strategies just as much. There were hints suggesting the interventions may be helpful in preventing relapse. There is an indication that the two interventions combined did not do any better than each on its own, but this requires replication in a larger study. Although the interventions show promise, the small number of participants recruited means we are unable to make strong conclusions. The study identified areas for future work.

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# Scientific Summary

**Background:** Most efforts to stop smoking that are initially successful end in relapse. Extended stop-smoking medication use can help prevent relapse, but uptake and long-term use are low. Fast acting nicotine replacement products such as nicotine mouth spray, lozenges, and also e-cigarettes, can be used opportunistically in relapse situations, which may be a more promising (and more economical) approach. Regarding behavioural interventions, whilst most approaches have been found ineffective, a recent trial of an online Structured Planning and Prompting Protocol (S3P), started at the beginning of the quit attempt, reduced relapse between one and 26 weeks.

**Objectives:** We planned to determine if the S3P combined with interactive texting, a provision of fast acting nicotine products to use in emergencies, and the combination of the two approaches, reduced relapse rates at 12 months post quit date compared to usual care; and to determine the feasibility and acceptability of the interventions and their cost effectiveness. The trial also included a qualitative and ecological momentary assessment sub study to explore the relapse process and barriers and facilitators to relapse prevention. Due to delays in setting up the online intervention as a result of technical and regulatory issues, problems with recruiting from Australian quitlines, and English service restructuring affecting recruitment, the trial was curtailed at six month follow up with a reduced sample size. As such, the revised (pre-specified) objective was whether the number of interventions received (none, one or two) affected relapse rates at six months post quit date.

**Design:** Multicentre RCT

**Participants and setting:** Originally, we planned to recruit 1400 recent ex-smokers, with 700 participants recruited from English stop smoking services and 700 from Australian quitlines. However, due to the issues described, only 234 participants were randomised (131 in Australia and 103 in England). Initially, participants were to be recruited when they had achieved at least four weeks of abstinence, but later participants in Australia were recruited from one week post quit date via social media and St Vincent’s Hospital, Melbourne.

**Study arms:** 1) A fast-acting nicotine product of the participant’s choice (nicotine mouth spray, lozenge, or e-cigarette) to use if at risk of relapse, accompanied by static text messages. 2) S3P: Participants received access to the online S3P that offers training in strategies to deal with temptations to smoke and provides motivational input. This was combined with intensive interactive text messaging. 3) Provision of both nicotine product and S3P interventions. 4) Static text messages added to usual care, typically comprising access to stop smoking medications used during the quit attempt for up to three months. (NB. Participants in all arms who were recruited through English stop smoking services and Australian quitlines also had access to their usual care alongside their allocated intervention.)

**Procedures:** Participants referred to the study were contacted by the study team to confirm eligibility, obtain consent and collect baseline data via online surveys or telephone. Participants were randomised to one of the four study arms following completion of the baseline survey. Participants in the nicotine product arm received their products by post, plus a series of static text messages (a maximum of 33 messages sent over 4 months). The S3P arm participants completed an online assessment which generated tailored advice, could complete new assessments for updated advice at any time, and also received a minimum of 55 interactive text messages over six months which were tailored to assessment responses. The usual care group received the same static messages as the nicotine product arm. Participants were followed up online or by telephone at three and six months. Ninety-four participants from the main study were also recruited to take part in a qualitative interview sub study. The interviews took approximately 30 minutes and were conducted by phone. The interviews were conducted following both the three and six month follow ups and included participants who had lapsed, relapsed and remained abstinent from each of the study arms. Data on the feasibility, acceptability, use and perceived impact of study interventions were collected. At around eight to 12 weeks post quit date 79 participants from the main study took part in an Ecological Momentary Assessment sub study, which involved four weeks’ monitoring of the use and relationship to cravings and slips of the two interventions using a handheld electronic diary.

**Measures and outcomes:** The original plan was to collect outcome data at three, six and 12 months post quit date, with biochemical validation of self-reported abstinence at 12 months. However, due to the curtailment of the study, outcome data were only collected at three and six months. All revised outcomes were pre-specified in the statistical analysis plan which was drafted prior to data download and analysis.

***Original primary outcome:*** Relapse rate in each study arm. Relapse was defined as smoking on at least seven consecutive days, or any smoking in the last month at 12 month follow up. Participants lost to follow-up were assumed to have relapsed.

***Curtailed primary outcome:*** Relapse rate in arms that received none (usual care), one (S3P or nicotine product), and two interventions (S3P plus nicotine product) at six months. Relapse was defined as smoking on at least seven consecutive days, or any smoking in the last month at six month follow up. Participants lost to follow-up were assumed to have relapsed.

***Original secondary outcomes:*** Sustained abstinence using different criteria to the primary outcome (e.g. point prevalence and shorter-term period prevalence outcomes), sustained reduction in cigarette consumption, evaluations of likely mechanisms of effect, focusing on strategies that were encouraged and participant perceptions of effect (e.g. participant ratings and data from EMA/qualitative sub studies), dose response effects, cost-effectiveness, effects of intervention components by country and by demographic, adverse events.

***Curtailed secondary outcomes:*** Sustained (no more than five cigarettes smoked since two weeks post quit date) and point prevalence (no smoking in the past seven days) abstinence at three and six months, nicotine product preferences (e.g. e-cigarette or NRT), product use at six months (frequency of use of nicotine, number of assessments completed for S3P, how many text messages read), use of coping strategies (pre-specified list with yes/no answers based on S3P strategies, plus EMA data), adverse events (freetext), participant ratings (e.g. 5 point scale: very useful to very useless) and qualitative feedback on the interventions.

**Sample size:** In our original sample size calculations, we expected that 70% of participants would relapse by 12 months in usual care, that each relapse prevention intervention would reduce the rate to 58%, and that the combination of the two interventions would result in a 48% relapse rate. Assuming no interaction and comparisons between those who received (two arms) and did not receive (two arms) each intervention individually, 257 participants were needed per arm to detect this difference (90% power, alpha=0.025, two-sided). We aimed to recruit 300 participants in each arm, with an additional 50 per arm for the ecological momentary assessment sub study. However, with our reduced sample size of 234, we used an alternative (pre-specified) approach that compared the number of interventions, i.e. none (UC), one (S3P or nicotine product), or two (nicotine product+S3P) and avoided multiple testing. Using 1-tailed alpha 0.05, the sample size afforded 78% power to detect the differences in relapse rates as estimated above. Ninety-four participants were recruited for the qualitative sub study and 79 were recruited for the ecological momentary assessment sub study.

**Results:** The six-month relapse rate was 60.0% (95%CI: 47% to 71%) in the usual care arm, 43.5% (95%CI: 35% to 53%) in those receiving one intervention (NIC: 44.8% 95%CI: 33% to 58%; S3P: 42.1% 95%CI: 30% to 55%) and 49.2% (95%CI: 37% to 62%) in those receiving two (p=0.11). The secondary outcome of sustained abstinence rates at six months were 41.7% in the usual care arm, 54.8% in those receiving one intervention (NIC: 53.5%; S3P: 56.1%), and 50.9% in those receiving two (p=0.17). In the two study arms which were offered a nicotine product, e-cigarette was chosen more frequently than NRT in Australia (71.0% versus 29.0%, p=0.001), but not in England (54.0% versus 46.0%, p=0.57). Most participants tried their products and 23.1% were still using them daily at six months (26.8% using e-cigarettes and 17.1% NRT). S3P received positive ratings (somewhat or very useful) from 63.0% of participants who provided the ratings at six months, regardless of whether or not the nicotine product intervention was added to S3P. Eighty-six percent of participants allocated to S3P completed at least one assessment, and over 60% of participants in the S3P arms also reported that they read the online advice, at least briefly. Overall the site was rarely re-visited and coping strategies imparted by S3P were used with similar frequency in all study arms. Only one participant used the S3P interactive texting feature. Tailored and static text messages received virtually identical ratings. The qualitative study suggested that access to the S3P intervention could be simplified.

**Limitations:** The inability to recruit sufficient participants resulted in lack of power to detect clinically relevant differences. Self-reported abstinence was not biochemically validated. The intervention started after a period of abstinence perhaps reducing the perceived relevance of interventions offered to participants. The study included some smokers who were only abstinent for seven days during their hospital stay.

**Conclusions:** Adherence to nicotine products was high and the online intervention was appreciated, but not widely used. There was a trend in favour of single treatments compared to usual care, but it did not reach statistical significance and the two interventions combined did not seem to be effective. The study is underpowered so further evaluation is warranted.

**Trial registration:** This trial was registered on the ISRCTN registry (ISRCTN11111428).

**Funding**: This project was funded by the National Institute for Health and Research (NIHR) Health Technology Assessment programme (HTA 13/155/05), UK and the National Health and Medical Research Council (NHMRC APP1095880), Australia. Public Health England (PHE) provided the funds to purchase the nicotine products in England.

**Key words:** relapse prevention, smoking, electronic cigarette, nicotine products, online intervention

**Word count:** 1649

# Chapter 1: Introduction

Material throughout the report has been adapted from the trial protocol by Hajek et al1.

Around 70% of smokers who quit in the short-term return to smoking within a year 2. The UK Government invests some £84.3 million annually to fund stop smoking services, not including the cost of smoking cessation medicines. The initial self-reported four week quit rates in smokers who engage in such treatment are around 50% 3, but in the longer term, the ubiquitous relapse substantially reduces the impact of these initiatives. As the health benefits of stopping smoking are primarily realised with long-term abstinence, relapse reduces the public health benefit of investment in smoking cessation interventions.

Preventing relapse to smoking has proven difficult. Two behavioural relapse prevention strategies have been formally evaluated: a ‘skills-based’ approach which focuses on teaching clients to identify relapse situations and put in place coping strategies 4, and extending the duration of the initial treatment with maintenance sessions to provide ongoing support. A systematic review from the Cochrane Collaboration 5 identified 81 relevant studies and concluded that despite good intuitive validity of these approaches, they showed no significant benefit. Another systematic review arrived at the same conclusion 6. The lack of benefit may be because clients do not learn the cognitive-behavioural skills or may not practice them, or the skills themselves may not be helpful at preventing relapse 7.

The Cochrane Review also identified 13 studies that examined the extended use of stop smoking pharmacotherapy 5. Extended use of varenicline (six months versus the standard three months; two studies) was associated with a small increase in one-year abstinence rates (RR = 1.23; 95% CI: 1.08-1.41), but no benefit was found for extended use of bupropion. Insufficient studies have evaluated effects of extended nicotine replacement therapy (NRT). Most successful quitters seem to have limited interest in continued use of currently licensed smoking cessation medicines over an extended period 8 9 and long-term use of these medicines also has substantial financial implications.

In 2014, the National Institute of Health Research commissioned a trial to further address this issue. The project was co-funded with the Australian National Health and Medical Research Council. The commissioned call specified a four-arm trial with a control, behavioural intervention, pharmacological intervention, and a combination of the two, to be conducted in England and Australia.

Our team identified two interventions that met these specifications and appeared worth evaluating.

Regarding behavioural support, extended support that requires that ex-smokers attend treatment sessions or maintain telephone contact is ineffective 5, most likely because successful quitters may not see the need to put effort into such contacts when they are not smoking, and once lapsed to smoking, may believe that there is no benefit in making contact or feel embarrassed to renew it. For example, in a trial where the provision of support relied on smokers taking the initiative to telephone the service when they felt in danger of lapsing or following a lapse, very few clients used the offer 10.

Information technology, in particular web-based resources and text messaging offers a more convenient way of providing ongoing support and is more consistent with the preference of many smokers to quit without using professional help 11. An online Structured Planning and Prompting Protocol (S3P), which provides tailored advice following online assessments with a particular focus on developing strategies for tempting situations in a form that helps ensure they will be remembered when needed, reduced relapse rates between one and 24 weeks from 71% to 61% 12. It is delivered online and can potentially be enhanced by mobile phone text messages. Texting interventions are inexpensive and can be easily disseminated on a large scale. The use of ongoing text-based contact to prevent relapse was piloted in 202 stop smoking service clients, who were abstinent four weeks after their quit date 9. Unlike invitations to attend sessions or call their advisors, the texting intervention was well received (70% of recent ex-smokers gave an overall score for helpfulness of the messages of 4 or 5 on a 5-point scale) and the retention rates were higher than with face-to-face or reactive telephone-based approaches. We aimed to evaluate an intervention combining the online coaching programme with text messaging.

Regarding pharmacological support, we discussed problems identified above related to persuading ex-smokers to continue using medications that they felt they did not need any more, and the financial implications of such long-term treatments. An alternative approach is to provide ex-smokers with medications to be used ‘in an emergency’. Fast-acting NRT such as nicotine mouth spray or lozenges seem well suited for this purpose. Another relatively new option is e-cigarettes. E-cigarettes have become popular among smokers 13 14 and there is increasing evidence supporting their effectiveness for smoking cessation 15 16. Some data are also emerging showing that e-cigarette use may help prevent relapse 17. In the pharmacological arm of the study, we aimed to evaluate the provision of ‘emergency supplies’ of clients’ choice of fast-acting NRT or an e-cigarette.

# Chapter 2: Methods

## Original and curtailed trial design

This was an individually randomised factorial trial including two interventions and usual care. The original plan was to recruit 1400 participants and follow them over 12 months. Due to circumstances described below, the trial was curtailed with 236 participants randomised and the follow-up period was reduced to six months.

## Changes to trial design/protocol (trial curtailment)

The trial encountered serious delays. The commencement of the trial was delayed as a result of the failure of the contracted IT consultants to deliver a version of the S3P program which, among other improvements and updates to the version trialled earlier, was to include data management capabilities (e.g. programming and scheduling of follow-up surveys, dynamic lists of scheduled calls for telephone interviewers, reminder emails, etc.). Unexpected technical issues and loss of staff with expertise were the primary reasons for this failure. The work had to be abandoned in April 2017, at which time we moved quickly to make necessary adaptations to the earlier version to the extent these were possible, and to program the data management aspects in REDCap® version 7.0.19 (Vanderbilt University Medical Centre, Nashville, USA). Integrating these two systems presented additional technical challenges. The integrated system was finally implemented in Australia in August 2017. UK regulations, however, did not allow the use of a system based abroad, and the integrated system had to be fully replicated and installed on a UK server. Experts responsible for implementing the Australian installation were not allowed direct access to it. The work proved difficult for local IT personnel and took some further six months to complete. During these delays, the English stop smoking services were subjected to substantial changes, which emerged as the next major problem for the study because of effects on client recruitment. Service management moved from the NHS to local councils who commissioned private providers, the stop smoking service throughput shrunk by over 60%, and few services remained that were able to contribute to such studies. Recruitment in Australia also proved difficult. The original plan was to recruit participants solely from the quitline in the state of Victoria. However, the number of participants they referred were far fewer than anticipated and so to help boost numbers, we sought to recruit more widely and the quitline from Tasmania agreed to take part. Despite this, referrals remained low. To boost recruitment in England, recruitment methods were expanded to include smokers quitting through the Stoptober campaign. In Australia, ex-smokers were approached via targeted Facebook ads and through St Vincent’s Hospital in Melbourne, recruiting patients who were discharged following a period of abstinence in hospital. The Australian site also expanded their recruitment window from 21-45 days post-quit to 7-100 days post quit. Despite these measures, the recruitment rate remained slow in both countries. After consultation with funders, it was decided to curtail the study. Recruitment was stopped in January 2019 and the decision was made to complete follow-ups at six rather than 12 months. Saliva sample collection, which had originally been planned to validate self-reports of abstinence at 12 months, and cost-effectiveness analyses, could not be carried out.

See Appendix 1, Tables 25 and 26 for details of changes to the protocol.

## Inclusion/exclusion criteria

**Inclusion Criteria**

* Smoking status: originally participants in England who had quit smoking with stop smoking services and participants in Australia who had quit smoking with quitlines, who were abstinent from smoking for at least two weeks and no more than 45 days at the point of recruitment. Later, participants from the Stoptober campaign were added in England (see Appendix 1, Table 25) and participants in Australia via Facebook or from St Vincent’s Hospital, Melbourne. In Australia the abstinence criteria was extended to at least one week and no more than 100 days quit at the point of recruitment (see Appendix 1, Table 26).
* Willing to use a nicotine product or online behavioural support tool if allocated to it
* Aged 18 years and older
* Owned a mobile phone
* Had Internet access
* Able to read/write/understand English

**Exclusion Criteria**

Participants were excluded if they were:

* Enrolled in other smoking cessation/relapse prevention research
* Currently using e-cigarettes or oral NRT and planning to use it for longer than three months

## Recruitment and setting

Planned recruitment was 1400 (700 in England and 700 in Australia). In total, 236 participants were randomised between September 2017 and January 2019. Two participants withdrew and requested their data not to be used, resulting in a total of 234 (131 in Australia and 103 in England).

In England, participants were originally recruited from six stop smoking services: Tower Hamlets, City of London, Leicester, Medway, Birkenhead and Durham. Later, those who had quit using the Stoptober 2018 campaign were also invited.

Participants in Australia were originally recruited from quitlines in Victoria and Tasmania and from March 2018 also from Facebook advertising and in the final months from among patients discharged from St Vincent’s Hospital, Melbourne.

Participants did not attend any face-to-face contact; interventions were delivered remotely (online and/or by telephone/mail/text messages). Follow up was completed online or by telephone calls conducted by researchers at the Health and Lifestyle Research Unit (England) and Cancer Council Victoria (Australia).

## Study Procedures

Potential participants from stop smoking services, Stoptober, quitlines and St Vincent’s Hospital were informed of the study by service staff and if interested, were given written information and referred to the research team. Potential participants from Facebook visited the study Facebook page and the associated study website where they self-referred.

Potential participants were contacted by email as soon as possible after referral. Those relapsing back to smoking before being reached were not invited to take part.

Participants were screened for eligibility online or over the phone, depending on their preference. Informed consent was also provided either online or verbally. Consenting participants completed a baseline survey (see Measures section below for details) and were randomised into one of four study arms (see Randomisation section below for details). Following this, the allocated treatment was initiated (see Interventions section below for details).

All participants were contacted by telephone about one week later to check that all was well, including that they had begun receiving text messages or received their chosen product. Any difficulties with the intervention were discussed and resolved.

## Interventions

Participants who, at randomisation, were using stop-smoking medications obtained from their service (e.g. NRT or varenicline), were encouraged to complete the course regardless of treatment allocation. In this report, we refer to these medications as ‘base medication’, unless they were similar fast-acting nicotine products as those we offered in the nicotine product intervention. That is, ‘base medication’ is defined as nicotine patches, varenicline or bupropion.

Common to all interventions was the provision of text messages provided for up to six months post quit. These included reinforcers of milestones, general motivational messages and some general hints. Non-S3P messages were non-interactive, untailored, and of lower frequency than the text messages provided in the S3P condition, which are described in more detail below.

**Usual care arm**

Participants received a text messaging program without any personalisation or reference to the specific strategies focused on in the S3P intervention. There was a maximum of 33 messages sent over six months (participants could request to stop the messages at any time). The usual care static text messages were not expected to have a clinically significant relapse prevention effect; thus this arm is considered for the purpose of analysis to have received no intervention. All non-S3P arms received these messages, in addition to any post-treatment care provided by stop-smoking services that delivered the initial stop-smoking interventions. Such interventions include an invitation to contact services if experiencing difficulties or lapses, although these are very rarely acted upon and would be present across randomisation groups.

**Nicotine product arm (NIC)**

Participants were given a choice of three oral nicotine products: Nicorette ® 1mg nicotine mouth spray (Johnson & Johnson Ltd, New Jersey, US); NiQuitin ® 4mg nicotine minis (**Omega Pharma Ltd, London, UK),** branded Nicabate ® 4mg nicotine minis in Australia (GlaxoSmithKline Australia Pty Ltd, Victoria, Australia), where an additional choice of 1.5 mg nicotine minis was offered as well; and a refillable e-cigarette (Innokin ® Endura T18E, Innokin Technology, Shenzen, China) with a choice of menthol or tobacco flavour liquid containing 11mg/ml nicotine. They chose one to use as a coping strategy if they found themselves at risk of relapse. The products were mailed to participants along with instructions on their use.

The initial supply comprised either an e-cigarette starter kit (including the refillable device, USB charger, spare battery, pack of 5 coils and four bottles of 10ml e-liquid, total cost £32.75), two bottles of nicotine mouth spray (total cost £17.95) or six tubs of minis (total cost £19.58).

In Australia, nicotine e-liquid is available on prescription only, and so if a participant requested an e-cigarette a local physician was asked by the study team to provide a prescription before the starter kit was sent to the participant.

Participants were offered further supply via an email/text about four weeks later. Those taking up the offer received four bottles of e-liquid, two bottles of mouth spray or six tubs of minis. Participants were able to switch to a different product for their second supply.

In England, participants who enquired about further supplies were asked to buy them themselves. To enable extended e-cigarette use in Australia, a note was sent with the second supply enabling participants to purchase further e-liquid and coils at a website managed by the study team via appropriate prescriptions.

The phone call about a week after randomisation checked product receipt and discussed product use as a strategy for coping with present or anticipated temptations to smoke.

Participants also received static text messages as per the usual care study arm (see above).

**S3P arm**

Participants completed a web-based assessment (QuitCoach), accessible from any web-enabled device but optimised for PC, that generated a three- to four-page letter of personalised advice. The advice included a list of priority activities with the prioritisation based on assessment responses. The letter could be viewed on screen in HTML or PDF format and printed if desired. It could be retrieved from the study website for later reference, until such time as a new assessment was commenced. New assessments were not mandatory; they were prompted by email, but participants could complete them at any desired time by returning to the study website. The resultant advice would then reflect their current situation and relevant progress since their previous assessment. In addition, participants could use a structured tool (Problem Planner) for generating if-then statements (implementation intentions, 18). Such self-generated statements link problematic situations (e.g. after dinner) with desired behavioural responses (e.g. staying inside and playing with the kids) and are designed to ensure that the appropriate response is triggered whenever the problematic situation is encountered. The Problem Planner could also be modified as frequently as desired.

The tailored advice contained separate strategies for those using and not using a nicotine product and provided general advice about countering more stable residual beliefs about the value of smoking, and suggestions for monitoring the ongoing benefits of having quit and taking appropriate rewards for reaching milestones.

The web-based intervention was augmented by a series of interactive text messages (QuitTxt) provided for up to six months post quit date, which further encouraged use of if-then statements, provided motivational messages, and gave some more generic advice. Unlike the non-S3P text messages, these text messages were tailored to baseline survey responses and to those from the most recent QuitCoach assessment, particularly to measures of difficulty staying quit (e.g. evidence of a recent slip-up, or frequent ongoing temptations to smoke). This primarily determined whether participants received the standard stream of 55 messages or an augmented stream of 72 messages. In addition to this, two special streams of messages were potentially sent:

(1) the “OFFMEDS” stream was a timed or user-triggered module designed to be sent either when people reported going off their base medication (i.e. bupropion, varenicline, or nicotine patches) or at around the time they indicated at baseline they would do so. Going off base medication was reported either via a QuitCoach assessment or an incoming SMS command (“OFFMEDS”). The OFFMEDS stream consisted of 17 messages and ran concurrently with the underlying standard or augmented stream.

(2) a “RELAPSE” stream was sent immediately upon notification of a relapse, either following an incoming “RELAPSE” command, or a QuitCoach assessment. The aim of this stream (12 messages) was to encourage immediate re-commitment to the quit attempt. Once completed, the underlying messages resumed with the augmented stream.

The text messaging program was able to respond to a variety of requests for additional help from the user. The commands were listed on a one-page PDF instruction form emailed to the user immediately following randomisation. In addition to “OFFMEDS” and “RELAPSE”, these took the form of ‘emergency help’ messages in response to commands such as “SOCIAL” or “STRESS”. These were designed to provide help in different forms of tempting situation, via an immediate message suggesting a strategy and a follow-up message half an hour later encouraging reflection. Any participant-requested additional messages were on top of the above-mentioned frequencies.

**Two Intervention arm (NIC+S3P)**

Participants received both interventions described above. The S3P advice and text messages were modified to include references to nicotine products as a relapse prevention strategy.

## Follow up

Follow up was originally planned for three, six and 12 months post quit date to record smoking status and other measures (see Measures section); however, due to the trial curtailment 12 month follow up was not completed. Participants had the option to complete the follow-ups over the phone or online. They received £10 for completing each of these questionnaires in England and $20 in Australia. The final follow ups took place between March 2018 and July 2019.

## Measures

At **baseline** we collected the following:

* Demographic details, smoking characteristics (heaviness of smoking index from when they were smoking 19, previous quit attempts, previous use of stop-smoking medications and e-cigarettes, and medical history (e.g. screening for depression, measures of perceived stress and affect)
* Information regarding the current quit attempt (including type of support/medicines used), frequency and strength of cravings, extent of slip-ups if any, plans on how long to continue use of base medication, self-efficacy for maintenance, perceived challenges, number of smokers in social network
* Quality of life as measured by the European Quality of Life-5 Dimensions (EQ5D) 20
* Health Service Use Questionnaire (HSUQ)

At all **follow up** contacts we collected:

* Self-reported smoking status and cigarette consumption
* Lapse/relapse details for those relapsing (number of lapses, when, where, reasons, how many cigarettes at first lapse, how soon after first cigarette was full relapse)
* Strategies used to prevent relapse
* Cravings to smoke
* Use of any, including non-allocated, smoking cessation/relapse prevention treatments
* Use and ratings of the allocated interventions, including helpfulness (three month follow up only)
* Adverse events

We also collected data regarding the use of the S3P, including number of assessments completed, number of text messages received, which message streams were received, and whether participants requested ‘emergency help’ messages or stopped the text messages.

At 12 month follow up we had planned to re-administer the EQ5D and HSUQ and collect saliva samples for cotinine analysis; however, due to the issues described earlier, follow up was terminated at six months and so these could not be collected. The baseline EQ5D and HSUQ data were therefore not analysed as there was no accompanying follow up data.

The curtailed schedule of measurements is shown in Table 1.

Table 1. Schedule of assessments

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Measures/Procedures** | **Three**  **weeks post quit date** | **Eight weeks post quit date** | **Three months post quit date** | **Six**  **months post quit date** |
| Demographics | X |  |  |  |
| Smoking history | X |  |  |  |
| Detail of current quit attempt | X |  |  |  |
| Randomisation and post randomisation phone call | X |  |  |  |
| Smoking status/cigarette consumption | X |  | X | X |
| Slip-ups and cravings | X |  | X | X |
| Use of non allocated products/interventions | X |  | X | X |
| Use and feedback of S3P (allocated cases only) |  |  | X |  |
| Use of allocated nicotine products (allocated cases only) | X |  | X | X |
| Ratings of interventions |  |  | X | X |
| EMA (sub study participants only, see Sub studies section) |  | X | X |  |
| Qualitative interviews (sub study participants only, see Sub studies section) |  |  | X | X |
| Health Service Use Questionnaire | X |  |  |  |
| Quality of life measures | X |  |  |  |
| Adverse events |  |  | X | X |

## Adverse Events (AEs) and Serious Adverse Event (SAEs)

Participants were asked about any AEs and SAEs experienced in the follow up surveys. In those allocated to the NIC arms, the following AEs were deemed to be related and expected in the study protocol: nausea, throat/mouth irritation and sleep disturbance.

## Sub studies

**Qualitative sub study**

The original plan was to recruit a sub sample of participants at each follow-up for qualitative interviews (N=160 in total, split equally between the two countries and four arms), using quota sampling to include participants who had lapsed/relapsed/maintained abstinence. Due to the issues described earlier, only 94 participants were recruited at three- and six-month follow-ups (see Figure 2 in the results section). Thus, a far greater proportion of the total sample than originally planned also participated in the qualitative sub study.

The qualitative study was conducted and reported in accordance with COREQ (‘COnsolidated criteria for REporting Qualitative’) research criteria 21. Data on the feasibility, acceptability, use and perceived impact of study interventions were collected from abstainers, lapsers and relapsers in the four trial arms from both countries. A topic guide (see Appendix 2) was developed by the research team and the non-trial related questions about relapse and relapse prevention were piloted in advance with two people who were former smokers and not connected to the study. The topic guide explored: how lapses influence relapse; triggers and context of lapses and relapses; barriers and facilitators to maintaining abstinence; and views in England and Australia on cessation and relapse prevention support.

Trial participants were advised upon recruitment into the main study that they might be invited into sub studies. Participants were asked at each follow-up whether they were willing to participate in the qualitative study. Those who agreed were grouped into relapsers (defined as smoking on seven or more consecutive days since recruitment into the main study), lapsers (defined as reporting any lapses – even a puff of a cigarette - but not relapsed) and complete abstainers. Within these categories, participants were selected based on filtering characteristics (e.g. age and sex distributions, arm of trial and outcome status) and invited by email, text and telephone to a telephone interview with a postdoctoral research associate (CE) trained in qualitative research methods. Those who agreed to take part gave verbal informed consent and a convenient time to conduct the interview was agreed. The interviews took approximately 30 minutes and were conducted by phone using Skype. The researcher introduced herself and explained that she was seeking to learn more about the participant’s experience of taking part in the relapse prevention trial and the process of relapse. The researcher was open with participants about her status as an ex-smoker if asked. Written field notes were taken throughout the interviews to retain to unanswered and unclear responses at the end of the interview, and also to help with contextualisation during analysis. The researcher had no prior contact with participants and no counselling was provided during the interviews. Interviews were recorded and transcribed. Participants received £20 ($40 in Australia). Those who participated after the three month survey (or refused) were not subsequently asked to participate at six months.

**Ecological Momentary Assessment (EMA) sub study**

We planned to recruit a subset of 50 participants from each arm (N=200 in total, split between the two countries) to take part in three weeks of EMA monitoring 22, which included detailed monitoring of the use and relationship to cravings and slips of the two interventions using a handheld electronic diary. However, due to the issues described earlier, only 79 participants were recruited (37 in England and 42 in Australia).

The monitoring took place immediately following the cessation of base medication, where applicable (for most participants this occurred approximately four to eight weeks after randomisation, eight to 12 weeks post quit date). During monitoring participants were asked to log every time they used a study nicotine product (if allocated to use), any lapses that occurred, and to respond to randomly scheduled prompts (four to five per day); additionally, they were asked to complete a daily morning and evening report.

The EMA device administered multiple types of questions across various assessments. The assessments included: baseline data, logging of cravings and/or slip-up cigarettes, detailed questions about a subsample of these situations, and daily reports of mood and overall coping. The detailed questions included an assessment of the participant’s current state (e.g. mood, withdrawal severity, craving etc.) as well as contextual and situational details (e.g. where the participant is, who they are with, what they are doing etc.), the trigger of the event (e.g. bad mood, smoking cues etc.) and the use of any behavioural coping strategies during the event. To avoid over-burdening participants with assessments, only a subset of reported events were sampled for full assessment. The device logged the time and date of events.

During the one-week post randomisation call for the main study, participants were invited to participate in the EMA study. At four to eight weeks post randomisation, those who had expressed an interest were consented and trained on EMA procedures over the phone. They were mailed the device with an instruction booklet.

Participants were contacted during the first three days of EMA monitoring to ensure they understood and were following procedures and received further EMA training as necessary. At the end of EMA monitoring the devices were posted back in pre-paid envelopes. Participants received £60 ($120 in Australia) for completing the study.

## Data management

**Data collection and entry**

Non-identifiable participant data were collected using the server on which the S3P intervention was run (for baseline data) and REDCap version 7.0.19 (for screening and follow up data). All data were kept in accordance with good clinical practice and data protection requirements.

**Data quality**

The English site checked completed electronic surveys on a weekly basis for anomalies and raised/resolved queries with the participant concerned. Once data collection was complete and data was cleaned the English and Australian datasets were merged.

## Sample size

In our original sample size calculation, we expected that 70% of participants would relapse by 12 months in usual care, that each relapse prevention intervention would reduce the rate to 58%, and that the combination of the two interventions would result in a further reduced 48% relapse rate. Assuming no interaction and comparisons between those who received (two arms) and did not receive (two arms) each intervention individually, 257 participants were needed per arm to detect this difference (90% power, alpha=0.025, two-sided). We aimed to recruit 300 participants in each arm, with an additional 50 per arm for the EMA study. However, with our reduced sample size of 234, we used an alternative, pre-specified approach that compared the number of interventions, i.e. none (UC), one (S3P or NIC), or two (NIC+S3P). Using 1-tailed alpha 0.05, the sample size afforded 78% power to detect the differences in relapse rates as estimated above, while avoiding multiple testing. This approach allows for utilising the information that the trial generated despite the limited power of the reduced sample, so that study data can contribute to any future meta-analyses.

## Randomisation

Participants were randomised, stratified by country in permuted blocks of random size, automatically via pre-programmed lists generated by the study statistician using Stata. The randomisation list was programmed into the server, on which the baseline survey was run by the study programmer, who had no involvement in the recruitment of participants. At the end of the baseline survey, the next unused entry on the list was selected and the participant was randomised accordingly. Subsequent on-screen prompts and questions were specific to each randomised condition.

## Treatment blinding

Researchers and participants were blind to allocation until the point or randomisation. Researchers conducting follow-up calls were not informed of the participants’ treatment allocation in their call lists and questions establishing relapse/abstinence outcomes were asked before condition-specific questions which could reveal the allocation. The trial statistician did not see the trial data (apart from recruitment updates) until data lock took place and remained blinded to participant allocation until analysis was complete.

## Statistical methods

***Main Study***

**Changes from planned analysis**

The planned analysis was changed due to trial curtailment. See the project webpage for the statistical analysis plan which includes details of the planned and curtailed trial analyses. The revised analyses were all pre-specified and agreed by the independent Data Monitoring and Ethics Committee (DMEC) prior to data download and analysis.

**General analysis principles**

The planned and actual main analysis for each outcome used the intention-to-treat (ITT) principle, meaning that all randomised participants were included in the analysis in the treatment group to which they were randomised. Participants with missing abstinence outcomes were considered smoking (relapsed) as per the Russell Standard 23.

In the curtailed study, the key study outcomes were analysed using a logistic regression where relapse status is regressed onto an ordinal predictor which codes the number of active interventions assigned (none, one, or two) adjusted for the stratifier (i.e. country). A one-sided p-value was used for the analysis of the primary outcome, and the significance level was set at 5%.

**Withdrawn participants**

Participants who did not wish to be followed up were withdrawn from the study. Unless they requested otherwise, data collected up to the point of their withdrawal was used in the study analysis and they were assumed to be smoking at later follow-ups.

***Qualitative sub study***

Transcribed interviews were indexed and imported into Nvivo 12 Pro for systematic analysis. The initial coding frame was based on the interview topic guides and new codes were added as they emerged from the data during the coding process. Coded data were then analysed using the ‘Framework’ method. This involves examining key themes from the interviews organised through ‘charting’ (see an example in Appendix 3). This allowed for investigation of participants’ views on relapse prevention interventions by treatment group. Interviewing stopped once a sense of thematic exhaustion and variability across the framework had accrued. What has been referred to as ‘theoretical saturation’ 24 occurred in the present study when significantly novel information relevant to the progression of thematic development and theorising ceased to emerge from the interview transcripts25 26. To enhance the validity of qualitative findings, two researchers were involved in all data analysis (CE and AM), and preliminary analyses were presented to the then UK Centre for Tobacco and Alcohol Studies (UKCTAS) Tobacco & Nicotine Group (current smokers or recent ex-smokers) for feedback.

***EMA Sub Study***

The EMA sub study was designed to provide data on the use of interventions and relationship to cravings and lapses for participants in the usual care and intervention arms at around eight to 12 weeks post quit date. While the reduced sample size did not allow for some of our originally planned analyses, we could conduct some exploratory analyses. Specifically: in order to explore the hypothetical mechanisms through which treatments can prevent relapse, we used the EMA data to examine group differences in the correlates of lapse episodes, and the immediate consequences of lapses, including self-efficacy and use of coping strategies. As each participant could contribute multiple lapse episodes, multilevel models were used to account for autocorrelation. This analysis plan is based on similar work exploring differences in lapse episodes between active and placebo patches 27.

In order to be eligible for this analysis, participants needed to report at least one lapse in real-time during monitoring. In total, 54 (68.4% of all the EMA sub study participants) reported at least one lapse event in real-time and were eligible for inclusion (UC: N=16; S3P: N=10; NIC: N=15; NIC+S3P: N=13).

# Chapter 3: Outcomes

**Original primary outcome**

Relapse rate at 12 months post quit date. Relapse was defined as self-report of smoking on seven or more consecutive days reported at any follow up, or any cigarettes smoked (even just a puff) in the last month, biochemically validated.

**Original secondary outcomes**

1a. Sustained abstinence using different criteria to the primary outcome and different assumptions about missing cases.

1b. Point prevalence and shorter-term period prevalence outcomes.

1c. Sustained reduction in cigarette consumption.

2. Evaluations of likely mechanisms of effect, focusing on strategies that were encouraged and participant perceptions of effect (e.g. participant ratings and data from EMA/qualitative sub studies).

3. Dose response effects. Testing whether the dose of the interventions, or extent of compliance, is associated with relapse.

4. Cost-effectiveness of the different strategies.

5. Effects of intervention components (e.g. on relapse rates, participant ratings etc.) by country and on people from different socioeconomic and ethnic groups, of different gender, with different prior smoking habits, and those who stopped smoking using different forms of medication.

6. Rates of adverse events/serious adverse events reported in people who use a study nicotine product compared to those who do not and by type of product used.

Due to the issues discussed earlier, the study outcomes were curtailed. All revised outcomes were pre-specified and agreed by the independent DMEC prior to data download and analysis.

## Curtailed primary outcome

Relapse rate at six months post quit date. Relapse was defined as self-report of smoking on seven or more consecutive days reported at either follow up, or any cigarettes smoked (even just a puff) in the last month at six months. Participants lost to follow-up were included as non-abstainers.

## Sensitivity analyses for primary outcome

To assess the robustness of the results, a series of sensitivity analyses were conducted, e.g. multiple imputation by chained equation 28 and complete case analysis where we excluded cases with missing outcomes. To build the multiple imputation model, we explored differences in baseline measures between participants with complete and missing outcome measures.

Per protocol analysis was conducted to exclude those participants who never accessed/used their allocated intervention. Initiation was coded as having tried the allocated product for NIC and NIC+S3P arms; having read at least one text for the usual care arm; having completed at least one assessment for the S3P and NIC+S3P arms. Missing data were counted as not initiated treatment.

## Curtailed secondary outcomes

1. Abstinence from smoking using alternative definitions: sustained abstinence (Russell Standard defined as self-report of not smoking more than five cigarettes since two weeks post quit date) and point prevalence abstinence at three and six months, defined as self-report of no smoking (not even a puff) in the past seven days.

2. Adherence to and ratings of the interventions by participants, and coping strategies used.

3. Characteristics of and reactions to lapses across the four groups explored in EMA/qualitative sub studies.

4. Rates of adverse events/serious adverse events reported in people who use a study nicotine product compared to those who do not.

## Statistical software

All analyses were carried out using Stata software version 15.

## Public and patient involvement (PPI)

Members of the UKCTAS public engagement panel and a member of the New Nicotine Alliance charity provided feedback on the study design and participant documents, and helped to inform the decision about which e-cigarette products to use. The Trial Steering Committee included members of the public, who contributed to decisions made regarding trial progress and curtailment.

## Trial committees

In England, a Trial Steering Committee and Data Monitoring and Ethics Committee were convened every six to 12 months. A Trial Management Group also met at regular intervals throughout the study. Appendix 1, Table 27 lists the trial committee members.

## Quality control and quality assurance

In England a risk assessment was carried out in conjunction with the study sponsor and Barts Clinical Trials Unit (CTU), now King’s CTU, which was used as a basis for the study monitoring plan. During the recruitment phase a monitor from the coordinating site carried out six monthly monitoring at the English site. The Barts CTU (now King’s CTU) was responsible for oversight of the monitoring process and overall audit of the trial.

## Approvals

The study was sponsored by the Queen Mary University of London (QMUL) Joint Management Research Office (JRMO) in England and the Cancer Council Victoria (CCV) in Australia.

Ethical approval was obtained from the National Research Ethics Service Committee London - Camden and Islington on 15 November 2016, reference 16/LO/1771 in England, and the CCV HREC (Project No. HREC 1606) on 15 August 2016 and the St Vincent’s Hospital Melbourne HREC (Ref no. HREC 092/18) on 6 August 2018 in Australia.

In Australia, the study was also notified to the Therapeutic Goods Administration, CTN No.: CT-2016-CTN-02901-1.

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# Chapter 4: Results

Throughout the results, characteristics and descriptive statistics are shown according to the four original study arms, but the analysis of relapse and abstinence is presented in three groups (none, one or two interventions), as per the pre-specified analysis plan for the curtailed trial.

## Participant flow

Figure 1 shows the flow of participants through the trial.

****Figure 1: Main study flow diagram RP trial****

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | |  | |  | | Screened for eligibility  (N=462) | | | |  |  |  | |  |
|  |  | |  |  | |  | |  |  |  | Not eligible (N=73)  Eligible but did not consent (N=123)  Eligible but did not complete baseline (N=30) | | | | |
|  |  | |  |  | |  | |  |  |  |
|  |  | |  |  | | Randomised N=236  (England: 105, Australia: 131) | | | | |  | |  |  |  |
|  |  | |  |  | |  | |  |  |  |  | |  |  |  |
|  |  | |  |  | |  | |  |  |  |  | |  |  |  |
| UC, N=60  Australia = 33  England = 27 | | |  | S3P, N=58  Australia = 32  England = 26 | | | |  |  | NIC, N=59  Australia = 33  England = 26 | | |  | NIC+S3P, N=59  Australia = 33  England = 26 | |
|  |  | |  |  | |  | |  |  |  |  | |  |  |  |
| Completed 3-month follow-up  N=53 | | |  | Completed 3-month follow-up  N=42 | | | |  |  | Completed 3-month follow-up  N=51 | | |  | Completed 3-month follow-up  N=51 | |
|  |  | |  |  | |  | |  |  |  |  | |  |  |  |
| Completed 6-month follow-up N=54 | | |  | Completed 6-month follow-up N=49 | | | |  |  | Completed 6-month follow-up N=52 | | |  | Completed 6-month follow-up N=52 | |
|  |  | |  |  | |  | |  |  |  |  | |  |  |  |
| Included in primary outcome N=60  Withdrew (included) N=1 | |  | | Included in primary outcome N=57  Withdrew (excluded)a N=1 | | | |  |  | Included in primary outcome N=58  Withdrew (excluded) a N=1  Withdrew (included), N=1 | | |  | Included in primary outcome N=59  Withdrew (included) N=1 | |

a did not wish for their data to be used in the study

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

## Sample characteristics

Table 2 shows participant characteristics. The sample comprised largely middle-aged smokers classified as ‘medium’ on the heaviness of smoking index. Less than half were in full employment and 28% reported a history of mental illness.

At the time of recruitment 49.1% of all participants reported using a base medication (69.9% and 32.8% of participants in England and Australia , respectively).

Table 2. Baseline characteristics

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Baseline characteristic** | **UC (N = 60)** | **NIC (N = 58)** | **S3P (N = 57)** | **NIC +S3P (N = 59)** |
| Age, years (N=234a), median (IQR) | 44 (34.5-55.5) | 46.5 (37-57) | 44 (35-56) | 43 (30-56) |
| Female, N (%) | 31 (51.7) | 26 (44.8) | 23 (40.3) | 32 (54.2) |
| Partner smokes:  Yes, N (%) | 7 (11.7) | 3 (5.2) | 8 (14.0) | 11 (18.6) |
| Mental health condition: Yesb, N (%) | 23 (38.3) | 16 (27.6) | 14 (24.6) | 12 (20.3) |
| In full time employment, N (%) | 24 (40.0) | 20 (34.5) | 24 (42.1) | 25 (42.4) |
| Receiving benefits, N (%) | 34 (56.7) | 32 (55.2) | 34 (59.7) | 29 (49.2) |
| Heaviness of Smoking Index, N (%)  Low  Medium  High | 7 (11.7)  42 (70.0)  11 (18.3) | 8 (13.8)  44 (75.9)  6 (10.3) | 9 (15.8)  34 (59.7)  14 (24.6) | 7 (11.9)  43 (72.9)  9 (15.3) |
| Using base medication, N (%) | 31 (51.7) | 24 (41.4) | 26 (45.6) | 34 (57.6) |
| Ethnicity (Australia):  Australian born (non-aboriginal), N (%) | 27 (81.8) | 24 (72.7) | 26 (81.3) | 27 (81.8) |
| Ethnicity (ENG):  White British, N (%) | 21 (77.8) | 22 (88.0) | 19 (76.0) | 22 (84.6) |
| Country, N (%)  AUS (n=131)  ENG (n=103) | 33 (55.0)  27 (45.0) | 33 (56.9)  25 (43.1) | 32 (56.1)  25 (43.9) | 33 (55.9)  26 (44.1) |

a N varies due to missing data

b Participants were able to respond, Yes, No, or Prefer not to answer

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Overall, follow-up rates were 88.5% at six months. This rate was similar in Australia (87.8%) and England (89.3%). Follow-up rates were also similar across arms: UC 90%, NIC 90%, S3P 86%, and NIC+S3P 88%.

Table 3 shows the missing data across primary and secondary outcomes, and Table 4 provides data on the differences in baseline characteristics between participants who provided primary outcome data and those who did not.

Table 3. Missing outcome data by study arm

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcome** | **UC (N = 60)** | **NIC (N = 58)** | **S3P (N = 57)** | **NIC+S3P (N = 59)** |
| Relapse at six months post quit, N (%) | 6 (10) | 6 (10.3) | 8 (14.0) | 7 (11.9) |
| Point prevalence abstinence at three months post quit, N (%) | 7 (11.7) | 7 (12.1) | 16 (28.1) | 8 (13.6) |
| Point prevalence abstinence at six months post quit, N (%) | 6 (10.0) | 6 (10.3) | 8 (14.0) | 7 (11.9) |
| Sustained abstinence at six months post quit, N (%) | 6 (10.0) | 6 (10.3) | 8 (14.0) | 7 (11.9) |

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Table 4. Differences in baseline characteristics between participants with complete versus missing primary outcome data

|  |  |  |
| --- | --- | --- |
| **Baseline characteristic** | **Complete (N=207)** | **Missing (N=27)** |
| Age, years, median (IQR) | 46 (33-57)  N=199 a | 39 (33-46)  N=25 a |
| Sex, N (%)  Female  Male | 103 (92.0)  104 (85.3) | 9 (8.0)  18 (14.8) |
| Partner smokes, N (%)  Yes  No  No spouse/partner | 27 (93.1)  96 (85.7)  84 (90.3) | 2 (6.9)  16 (14.3)  9 (9.7) |
| Mental health condition, N (%)  Yes  No  Prefer not to answer | 62 (95.4)  139 (86.3)  6 (75.0) | 3 (4.6)  22 (13.7)  2 (25.0) |
| Employment status, N (%)  Full time  Part time  Neither | 79 (85.0)  32 (86.5)  96 (92.3) | 14 (15.0)  5 (13.5)  8 (7.7) |
| Receiving benefits, N (%)  Yes  No | 115 (89.2)  92 (87.6) | 14 (10.9)  13 (12.4) |
| Heaviness of Smoking Index, N (%)  Low  Medium  High | 28 (90.3)  144 (88.3)  35 (87.5) | 3 (9.7)  10 (11.7)  5 (12.5) |
| Using base medication, N (%)  Yes  No | 99 (86.1)  108 (90.8) | 16 (13.9)  11 (9.2) |
| Ethnicity – AUS N (%)  Australian born (non-aboriginal)  Other | 90 (86.5)  25 (92.6)  N=115 a | 14 (13.5)  2 (7.4)  N=16 a |
| Ethnicity – ENG, N (%)  White  Other | 74 (88.1)  18 (94.7)  N=92 a | 10 (11.9)  1 (5.3)  N=11 a |
| Country, N (%)  AUS  ENG | 115 (87.8)  92 (89.3) | 16 (12.2)  11 (10.7) |

a N varies due to missing data

b Participants were able to respond, Yes, No, or Prefer not to answer

## Relapse rates

Relapse to smoking was somewhat higher in usual care than in the individual or combined interventions but the combined intervention did not show any trend to higher efficacy compared to single interventions. The overall difference was not significant (p=0.11), see Table 5.

Table 5. Relapse rate at six months post quit

|  |  |
| --- | --- |
| **Arms** | **N (%) who relapsed** |
| UC (no intervention) | 36 (60.0) |
| NIC or S3P (one intervention)  *NIC*  *S3P* | 50 (43.5)  *26 (44.8)*  *24 (42.1)* |
| NIC+S3P (two interventions) | 29 (49.2) |

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

The results of the sensitivity analyses of the primary outcome tallied with the main analyses (Table 6).

To provide more descriptive information we also looked at the relative risks for reducing relapse in each of the arms, using the usual care arm as the reference. These were 0.75 (95%CI: 0.53 to 1.06), 0.70 (95%CI: 0.48 to 1.00) and 0.83 (95%CI: 0.60 to 1.14) for the NIC, S3P and NIC+S3P arms, respectively.

Table 6. Primary analysis and sensitivity analyses of relapse rates at six months

|  |  |  |
| --- | --- | --- |
| **Type of Analysis** | **N (%)** | **Likelihood of relapse associated with one intervention increase**  **RR (95%CI)** |
| Primary Analysis | 234 | 0.88  (0.73- 1.07) |
| Complete cases | 207 | 0.84  (0.67- 1.06) |
| Multiple imputation a | 234 | 0.87  (0.69- 1.1) |
| Participants who initiated treatment b | 206 | 0.83  (0.65- 1.07) |

a Missing information on the primary outcome was estimated using multiple imputation (MI) by chained equations. MI relies on the assumption that data are missing at random (MAR). To increase the likelihood of the MAR assumption and improve the estimation of the non-missing values, we included variables associated with the primary outcome as well as its “missingness” in our model and secondary outcomes measuring smoking status at various time points including baseline. The auxiliary variables included baseline characteristics (i.e. sex, age, country, partner smoking status, mental health status), adherence to treatment, number of follow-up surveys completed, and mechanisms to remain abstinent (e.g. whether participants rewarded themselves for not smoking and ways with dealing with temptation).

b Initiation is coded as having tried the allocated product for NIC or NIC+S3P arms; having read at least one text for the UC arm; having completed at least one assessment for the S3P or NIC+S3P arms. Missing data is counted as not initiated treatment.

## Sustained and seven-day point prevalence abstinence rates

Table 7 shows sustained abstinence rates as defined by the Russell Standard (allows up to five lapses) and point prevalence abstinence rates (no smoking over the past seven days). There were no significant differences between the study arms.

Table 7. Sustained and seven-day abstinence rates

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcome** | **No intervention (UC)**  **N = 60** | **One intervention**  **(NIC or S3P)**  **N=115**  **[NIC: N=58; S3P: N=57]** | **Two interventions**  **(NIC+S3P)**  **N = 59** | **Likelihood of abstinence associated with one intervention increase**  **RR (95%CI)** |
| Seven-day abstinence at three months N (%) [95% CI] | 37 (61.7) [49-73] | 77 (67.0)  [60-75]  *NIC: 42 (72.4)*  *[60-82]*  *S3P: 35 (61.4)*  *[48- 73]* | 38 (64.4)  [52- 76] | 1.03  (0.91- 1.17) |
| Seven-day abstinence at six months N (%) [95% CI] | 36 (60.0)  [47-71] | 75 (65.2)  [56-73]  *NIC: 35 (60.3)*  *[48-72]*  *S3P: 40 (70.2)*  [57-81] | 36 (61.0)  [48-72] | 1.01  (0.89- 1.16) |
| Sustained abstinence at six months N (%) [95% CI] | 25 (41.7)  [30-54] | 63 (54.8)  [46-64]  *NIC: 31 (53.5)*  *[41-66]*  *S3P: 32 (56.1)*  *[43-68]* | 30 (50.9)  [38-63] | 1.09  (0.92- 1.29) |

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

## Treatment adherence and use of allocated treatments

Nicotine product selection by arm and by country is shown in Tables 8 and 9. More participants chose e-cigarette than NRT (63.4% versus 36.6%), chi-square(1)=8.04, p=.005.

In Australia, 71.0% chose e-cigarette versus 29.0% who chose NRT; chi-square(1)=10.9, p=.001. In England, there was no significant difference in the number of participants choosing e-cigarette versus NRT (54.0% versus 46.0%; chi-square(1)=0.3, p=.57).

Of those who chose NRT, nicotine minis and mouth spray were selected with similar frequency within NIC arms and countries.

Table 8. Nicotine product choice by arm

|  |  |  |  |
| --- | --- | --- | --- |
| **Product chosen** a**, N (%)** | **NIC (N = 55)** | **NIC+S3P (N = 57)** | **Total (N=112)** |
| E-cigarette | 31 (56.4) | 40 (70.2) | 71 (63.4) |
| NRT | 24 (43.6) | 17 (29.8) | 41 (36.6) |

a Product choice is missing for three participants in the NIC arm and two participants in the NIC+S3P arm

S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Table 9. Nicotine product choice by country

|  |  |  |
| --- | --- | --- |
| **Product chosen** a**, N (%)** | **Australia (N = 62)** | **England (N = 50)** |
| E-cigarette | 44 (71.0) | 27 (54.0) |
| NRT | 18 (29.0) | 23 (46.0) |

a Product choice is missing for four participants in Australia and one participant in England

Table 10 shows the use of and adherence to the study nicotine products. At three months, over 50% of participants in the NIC and NIC+S3P study arms reported using their product at least occasionally. At six months, this applied to 40%. Among participants who chose e-cigarette, 26.8% were using them daily at six months, while 17.1% of participants who used NRT were using them daily at six months.

Most participants (N=66, 58.9%) requested and were sent a second supply of nicotine product.

With regards to continued use of any oral nicotine products in the non-NIC arms, at six months the proportions were 16 (26.7%) and 13 (22.8%) in the usual care and S3P only arms respectively. In the usual care arm, 15 (25.0%) were using oral NRT and 2 (3.3%) were using e-cigarette (one participant was using both oral NRT and e-cigarette). In the S3P only arm 12 (21.1%) were using oral NRT and 1 (1.8%) were using e-cigarette.

Table 10. Use of and adherence to NIC intervention

|  |  |  |  |
| --- | --- | --- | --- |
| **Measure of use/adherence** | **NIC** | **NIC+S3P** | **Total** |
| NIC product use at three months post quit, N (%) e  *Never used*  *Tried b*  *Used but now stopped c*  *Using some days*  *Using daily* | N=58  4 (6.9)  9 (15.5)  7 (12.1)  10 (17.2)  20 (34.5) | N=59  7 (11.9)  7 (11.9)  4 (6.8)  16 (27.1)  16 (27.1) | N=117  11 (9.4)  16 (13.7)  11 (9.4)  26 (22.2)  36 (30.8) |
| NIC product at six months post quit, N (%) e  *Not using*  *Using some days*  *Using daily*  *Using, frequency unknown*  Daily use at 6 months by product, N (%) d, e  *E-cigarette*  *NRT* | N=58  30 (51.7)  5 (8.6)  16 (27.6)  1 (1.7)  10 (32.3)  N=31  5 (20.8)  N=24 | N=59  27 (45.8)  11 (18.6)  11 (18.6)  3 (5.1)  9 (22.5)  N=40  2 (11.8)  N=17 | N=117  57 (48.7)  16 (13.7)  27 (23.1)  4 (3.4)  19 (26.8)  N=71  7 (17.1)  N=41 |

a Percentages do not add up to 100% due to missing data (participants not responding to survey).

b ‘Tried’ defined as ‘tried but no further need’ and ‘used once or twice’

c ‘Used’ defined as ‘used on a number of occasions’

d Product choice unknown for one respondent in each arm

e Refers specifically to the study NIC products (e.g. mouth spray, lozenge or e-cigarette), not use of other nicotine products

S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Table 11 shows the use of and adherence to the S3P. Most participants allocated to the S3P intervention completed one QuitCoach assessment only.

At three months, most respondents in the S3P arms reported having read the advice generated by the intervention, with the majority responding, ‘Yes, but only quickly’. Only a third of participants in the S3P arms reported having used the Problem Planner (Table 11).

Table 11. Use of and adherence to the S3P (S3P arms only)

|  |  |  |
| --- | --- | --- |
| **Measure of use/adherence** | **S3P**  **(N=57)** | **NIC+S3P**  **(N=59)** |
| **Number of QC assessments completed, N (%)**  *0*  *1*  *2*  *3*  *5*  *6* | 7 (12.3)  35 (61.4)  9 (15.8)  4 (7.0)  1 (1.8)  1 (1.8) | 9 (15.3)  37 (62.7)  7 (11.9)  3 (5.1)  3 (5.1)  0 (0) |
| **Did you read the QuitCoach advice? a N (%)**  Yes, I studied it carefully  Yes, but only quickly  No | 12 (21.1)  19 (33.3)  8 (14.0) | 19 (32.2)  26 (44.1)  6 (10.2) |
| **Did you use the Problem Planner? a N (%)**  Yes, quite a lot  Yes, a bit  No | 0 (0)  14 (24.6)  17 (29.8) | 1 (1.7)  22 (37.3)  23 (39.0) |

a Percentages do not add up to 100 due to missing data (participants not responding to survey).

S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Table 12 shows the use of the text messages. Most responders reported reading all/most of the text messages sent. Roughly the same small proportion of participants (12% maximum) requested to stop the text messages across the study arms, though this was least in the NIC only arm (5.2%).

A feature of the S3P arms was the interactive element of the text messages. Only one participant (in the S3P only arm) used the interactive text message commands, sending the following: “STRESS” (four times), “SOCIAL” (twice), “MISSING SMOKING” (twice) and “TEMPTATION” (twice).

Table 12. Use of and adherence to text messages (all arms)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Measure of use/adherence** | **UC**  **N=60** | **NIC**  **N=58** | **S3P**  **N=57** | **NIC+S3P**  **N=59** |
| Read most/all texts, N (%) | 35 (58.3) | 38 (65.5) | 28 (49.1) | 36 (61.0) |
| Requested to stop text messages, N (%) | 6 (10.0) | 3 (5.2) | 6 (10.5) | 7 (11.9) |

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

## Ratings of S3P intervention

Participant ratings of the S3P intervention at three and six months are shown in Tables 13 and 14.

At three months, the most common rating for the S3P was ‘somewhat useful’, with median rating of 2 (IQR = 2 to 3) in the S3P and 2 (IQR = 2 to 3) in the NIC+S3P arm. At six months, ratings seemed to improve in the S3P only arm (median rating 1 (IQR = 1 to 3)) while remaining the same in the NIC+S3P arm (median rating 2 (IQR = 2 to 3)). Most participants considered the intervention useful but only a quarter of responders said they would visit QuitCoach again.

Table 13. Rating of QuitCoach at three and six months post quit

|  |  |  |
| --- | --- | --- |
| **QuitCoach rating** | **S3P, N (%)** | **NIC+S3P, N (%)** |
| **Three months post quit date** | **(N = 28)** | **(N = 43)** |
| Very useful | 5 (17.8) | 10 (23.3) |
| Somewhat useful | 10 (35.7) | 19 (44.2) |
| Neither | 9 (32.1) | 11 (25.6) |
| Somewhat useless | 4 (14.3) | 6 (7.0) |
| Very useless | 0 (0) | 0 (0) |
| **Six months post quit date** | **(N = 48)** | **(N = 52)** |
| Very useful | 15 (31.3) | 12 (23.1) |
| Somewhat useful | 12 (25.0) | 24 (46.2) |
| Neither | 13 (27.1) | 11 (21.2) |
| Somewhat useless | 3 (6.3) | 1 (1.9) |
| Very useless | 5 (10.4) | 4 (7.7) |

S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Table 14. Answer to the question “would you visit QuitCoach again?” at three months post quit

|  |  |  |
| --- | --- | --- |
| **Response to question** | **S3P, N (%)**  **N=28** | **NIC+S3P, N (%)**  **N=43** |
| Yes | 6 (21.4) | 14 (32.6) |
| Not sure | 17 (60.7) | 19 (44.2) |
| No | 5 (17.9) | 19 (23.3) |

S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Table 15 shows the ratings of the text messages. Despite different contents and intensity of the text messages and the tailoring and interactive features of messages in the S3P condition, ratings were similar across the four study arms.

Table 15. Rating of text messages at three and six months post quit

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Text message rating** | **UC, N (%)** | **NIC, N (%)** | **S3P, N (%)** | **NIC+S3P N (%)** |
| **Three months post quit** | **(N = 48)** | **(N = 50)** | **(N = 38)** | **(N = 50)** |
| Very useful | 13 (27.1) | 17 (34.0) | 11 (29.0) | 15 (30.0) |
| Somewhat useful | 15 (31.3) | 25 (50.0) | 14 (36.8) | 20 (40.0) |
| Neither | 5 (10.4) | 1 (2.0) | 6 (15.8) | 10 (20.0) |
| Somewhat useless | 7 (14.6) | 3 (6.0) | 3 (7.9) | 3 (6.0) |
| Very useless | 8 (16.7) | 4 (8.0) | 4 (10.5) | 2 (4.0) |
| **Six months post quit** | **(N = 53)** | **(N = 52)** | **(N = 48)** | **(N = 52)** |
| Very useful | 16 (30.2) | 21 (40.4) | 12 (25.0) | 13 (25.0) |
| Somewhat useful | 19 (35.9) | 17 (32.7) | 14 (29.2) | 21 (40.4) |
| Neither | 5 (9.4) | 5 (9.6) | 9 (18.8) | 8 (15.4) |
| Somewhat useless | 6 (11.3) | 4 (7.7) | 4 (8.3) | 3 (5.8) |
| Very useless | 7 (13.2) | 5 (9.6) | 9 (18.8) | 7 (13.5) |

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

## Use of S3P recommended strategies

Behavioural strategies specifically recommended in the S3P intervention were used across all four study arms (see Tables 16-18). Across the strategies suggested, the S3P arms did not consistently report more use than the non-S3P arms.

Table 16. S3P strategies used at three and six months post quit

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Strategies used at three months post quit** | **UC, N (%)** | | **NIC, N (%)** | | **S3P, N (%)** | | **NIC+S3P, N (%)** | |
| **Three months** | **Six months** | **Three months** | **Six months** | **Three months** | **Six months** | **Three months** | **Six months** |
| Remind myself of reasons for quitting (N=191, N=201)a | 46 (90.2)  N=51 | 47 (90.4)  N=52 | 40 (80.0)  N=50 | 47 (94.0)  N=50 | 38 (97.4)  N = 39 | 45 (93.8)  N = 48 | 43 (84.3)  N = 51 | 45 (88.2)  N = 51 |
| Distracted myself by doing something else (N=191, N=201) a | 44 (86.3)  N=51 | 42 (80.8)  N=52 | 38 (76.0)  N=50 | 35 (70.0)  N=50 | 33 (84.6)  N = 39 | 39 (81.3)  N = 48 | 41 (80.4)  N = 51 | 42 (82.4)  N = 51 |
| Put in place a plan I had for resisting (N=191,  N=200) a | 19 (37.3)  N=51 | 18 (35.3)  N=51 | 22 (44.0)  N=50 | 19 (38.0)  N=50 | 10 (25.6)  N = 39 | 15 (31.3)  N = 48 | 18 (35.3)  N = 51 | 20 (39.2)  N = 51 |
| Just tried to ignore it (N=190,  N=200) a | 42 (84.0)  N=50 | 39 (76.5)  N=51 | 44 (88.0)  N=50 | 42 (84.0)  N=50 | 31 (79.5)  N = 39 | 43 (89.6)  N = 48 | 38 (74.5)  N = 51 | 38 (74.5)  N = 51 |
| Just waited until the craving went away (N=190,  N=200) a | 34 (68.0)  N=50 | 33 (64.7)  N=51 | 38 (76.0)  N=50 | 37 (74.0)  N=50 | 28 (71.8)  N = 39 | 34 (70.8)  N = 48 | 35 (68.6)  N = 51 | 34 (66.7)  N = 51 |
| Told myself that I am beating my addiction (N=190, N=201) a | 31 (62.0)  N=50 | 31 (59.6)  N=52 | 36 (72.0)  N=50 | 34 (68.0)  N=50 | 23 (59.0)  N = 39 | 32 (66.7)  N = 48 | 34 (66.7)  N = 51 | 36 (70.6)  N = 51 |
| Some other strategy (N=191,  N=200) a | 19 (37.3)  N=51 | 12 (23.5)  N=51 | 15 (30.0)  N=50 | 13 (26.0)  N=50 | 8 (20.5)  N = 39 | 11 (22.9)  N = 48 | 12 (23.5)  N = 51 | 13 (25.5)  N = 51 |

a Three and six months respectively

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

The S3P intervention included a suggestion for clients to make a list of reasons for quitting and to consult it when tempted to smoke. Somewhat surprisingly, participants in the usual care and NIC arms reported doing this to a similar extent as those who received the intervention (see Table 17).

Table 17. Responses to ‘Did you make a list of your reasons for quitting?’ at three months post quit

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Made a list of reasons for quitting at three months post quit, N (%)** | **UC**  **(N = 50)** | **NIC**  **(N=50)** | **S3P**  **(N = 39)** | **NIC+S3P**  **(N = 51)** |
| Yes, and I remind myself | 15 (30.0) | 17 (34.0) | 15 (39) | 12 (23.5) |
| Yes, but I never look at it | 5 (10.0) | 12 (24.0) | 11 (28.2) | 12 (23.5) |
| No | 30 (60.0) | 21 (42.0) | 13 (33.3) | 27 (52.9) |

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

The S3P also encouraged clients to give themselves rewards for achieving milestones at three and six months. This too was done just as frequently in non-S3P study arms (see Table 18).

Table 18. Responses to ‘Have you been giving yourself rewards for achieving milestones?’ at three and six months post quit date

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Rewards given at three months post quit** | **UC**  **(N = 50)** | **NIC**  **(N = 50)** | **S3P**  **(N = 39)** | **NIC+S3P**  **(N = 51)** |
| Yes, N (%) | 24 (48.0) | 32 (64.0) | 22 (56.4) | 30 (58.8) |
| **Rewards given at six months post quit** | **UC**  **(N = 36)** | **NIC**  **(N=30)** | **S3P**  **(N = 33)** | **NIC+S3P**  **(N = 35)** |
| Yes, N (%) | 19 (52.8) | 18 (60.0) | 16 (48.5) | 16 (45.7) |

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

## Adverse events (AEs)

At three months numerically more participants reported AEs in the usual care arm than in intervention arms, (25% in the usual care versus 12.1%, 15.8% and 10.2% for the NIC, S3P and NIC+S3P arms respectively), see Table 19.

At six months the numbers of participants reporting AEs were similar across all study arms (Table 21).

Severe AEs were uncommon (reported by 6.0% of participants at three months and 3.9% at six months), see Tables 19 and 20.

There were eight serious adverse events (SAEs) reported across six participants: UC: arm surgery, incarcerated umbilical hernia; S3P: anorexia, car accident; NIC+S3P: gallstones; mastectomy with breast reconstruction, later resulting in emergency breast reconstruction removal, and tarsometatarsal fusion. None of the events were deemed related to study procedures.

Table 19. Adverse events reported at three months post quit

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **UC** | **NIC** | **S3P** | **NIC+S3P** | **Total** |
|  | **(N = 60)** | **(N = 58)** | **(N = 57)** | **(N = 59)** | **(N = 234)** |
| **Yes to an adverse event a** | 15 (25.0) | 7 (12.1) | 9 (15.8) | 6 (10.2) | 37 (15.8) |
| **Yes to a severe adverse event** | 5 (8.3) | 3 (5.2) | 4 (7.0) | 2 (3.4) | 14 (6.0) |
| **Adverse event listed b** |  |  |  |  |  |
| Anaemia vitamin B12 deficiency |  |  | 1 |  | 1 |
| Anorexia nervosa |  |  | 1 |  | 1 |
| Anxiety | 3 |  | 1 |  | 4 |
| Bursitis |  | 1 |  |  | 1 |
| Cough | 2 |  | 1 | 1 | 4 |
| Depressed mood | 1 |  |  |  | 1 |
| Depression |  | 1 |  |  | 1 |
| Diabetes mellitus |  |  |  | 1 | 1 |
| Diarrhoea |  |  |  | 1 | 1 |
| Disturbance in attention | 1 |  |  |  | 1 |
| Dysphagia | 1 |  |  |  | 1 |
| Dyspnoea | 4 | 1 |  | 1 | 6 |
| Eczema |  |  | 1 |  | 1 |
| Epilepsy |  |  | 1 |  | 1 |
| Fatigue | 1 |  |  | 1 | 2 |
| Folate deficiency |  |  | 1 |  | 1 |
| Gastritis |  | 1 |  |  | 1 |
| Headache | 3 |  |  |  | 3 |
| Hernia |  | 1 |  |  | 1 |
| Hypermobility syndrome |  |  | 1 |  | 1 |
| Immunodeficiency | 1 |  |  |  | 1 |
| Influenza | 1 |  |  |  | 1 |
| Insomnia | 1 | 2 |  |  | 3 |
| Lower respiratory tract infection | 1 |  |  |  | 1 |
| Mental disorder | 1 |  |  |  | 1 |
| Micturition disorder |  |  | 1 |  | 1 |
| Mouth ulceration |  |  |  | 1 | 1 |
| Multiple sclerosis |  |  |  | 1 | 1 |
| Oropharyngeal pain |  | 1 |  |  | 1 |
| Palpitations |  | 1 |  |  | 1 |
| Paraesthesia | 1 |  |  |  | 1 |
| Pertussis |  | 1 |  |  | 1 |
| Respiration abnormal |  | 1 |  |  | 1 |
| Restlessness |  |  |  | 1 | 1 |
| Rhinorrhoea | 1 |  |  |  | 1 |
| Sciatica | 1 | 1 |  |  | 2 |
| Sleep disorder |  |  |  | 1 | 1 |
| Weight increased | 1 | 1 | 2 | 2 | 6 |

a Missing items are interpreted as absence of adverse event.

**b** Patients reported up to five items so the total count of items is greater than the number of participants experiencing adverse events.

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Table 20. Adverse events reported at six months post quit date

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **UC** | **NIC** | **S3P** | **NIC+S3P** | **Total** |
|  | **(N = 60)** | **(N = 58)** | **(N = 57)** | **(N = 59)** | **(N = 234)** |
| **Yes to an adverse event a** | 12 (20.0) | 11 (19) | 10 (17.5) | 12 (20.3) | 45 (19.2) |
| **Yes to a severe adverse event** | 3 (5.0) | 1 (1.7) | 2 (3.5) | 3 (5.1) | 14 (3.9) |
| **Adverse events listed b** |  |  |  |  |  |
| Anaemia vitamin B12 deficiency |  |  | 1 |  | 1 |
| Anorexia nervosa |  |  | 1 |  | 1 |
| Anxiety | 1 |  |  | 1 | 2 |
| Atrial fibrillation |  |  | 1 |  | 1 |
| Back pain |  |  | 1 | 1 | 2 |
| Blood cholesterol increase | 1 |  |  |  | 1 |
| Blood pressure increase | 1 | 1 |  |  | 2 |
| Bursitis |  | 1 |  |  | 1 |
| Chest discomfort |  | 1 |  |  | 1 |
| Cholelithiasis |  |  |  | 1 | 1 |
| Chronic obstructive pulmonary disease | 1 |  | 2 | 1 | 4 |
| Cough |  | 2 |  |  | 2 |
| Depression |  | 1 |  |  | 1 |
| Dyspnoea | 2 |  |  | 1 | 3 |
| Eczema |  |  | 1 |  | 1 |
| Endometrial hyperplasia |  |  |  | 1 | 1 |
| Epilepsy |  |  | 1 |  | 1 |
| Fatigue | 2 |  |  |  | 2 |
| Folate deficiency |  |  | 1 |  | 1 |
| Frequent bowel movement |  |  |  | 1 | 1 |
| Gingivitis |  |  |  | 1 | 1 |
| Headache |  | 1 |  | 1 | 2 |
| Increased umbilical hernia | 1 |  |  |  | 1 |
| Injury |  | 1 |  |  | 1 |
| Insomnia |  | 1 |  |  | 1 |
| Intervertebral disc degeneration | 1 |  |  |  | 1 |
| Lower respiratory tract infection |  |  | 1 |  | 1 |
| Malaise |  |  | 1 |  | 1 |
| Mental disorder |  | 1 |  |  | 1 |
| Mood altered |  | 1 |  |  | 1 |
| Parkin’s disease | 1 |  |  |  | 1 |
| Renal cyst |  |  |  | 1 | 1 |
| Rhinorrhoea |  |  | 1 | 1 | 2 |
| Sleep apnoea syndrome |  |  |  | 1 | 1 |
| Surgery | 1 |  |  |  | 1 |
| Thyroid gland disorder |  |  | 1 |  | 1 |
| Vitamin D deficiency | 1 |  |  |  | 1 |
| Von Willebrand’s |  |  |  | 1 | 1 |
| Weight increased | 1 | 1 | 2 | 1 | 5 |

a Missing items are interpreted as absence of adverse event.

**b** Patients reported up to four items so the total count of items is greater than the number of participants experiencing adverse events.

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

**Participation in the qualitative and EMA sub studies**

The qualitative and EMA sub studies were originally planned to involve only a small sub-sample of a large trial, with identical sampling across study arms. In the curtailed study, a much larger proportion of the sample took part in qualitative interviews (40%, N=94) and about a third of participants (N=79) took part in the EMA study. Of these, 48 people participated in both.

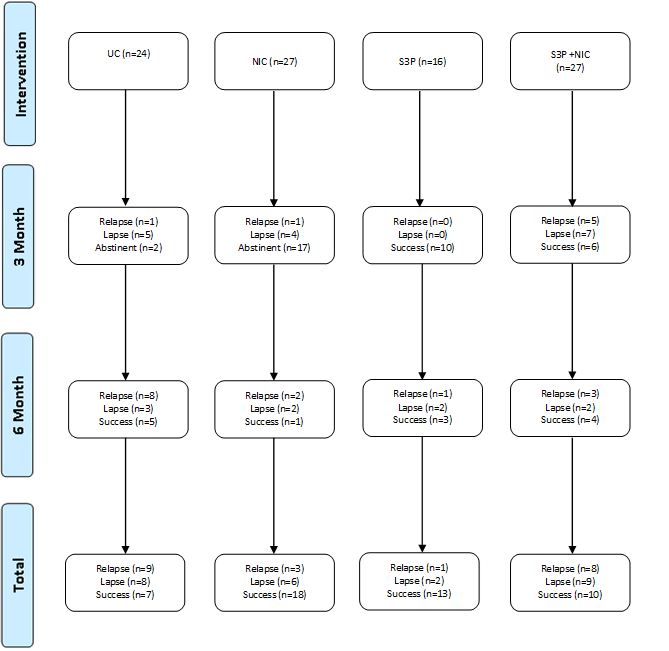
Relapse rates were lower among those participating in the sub studies (qualitative = 21.7%; EMA = 10.4%, and qualitative + EMA = 16.5%) than those who did not participate (51.3%).

The results of these sub studies are presented in chapters 5 and 6.

# Chapter 5: Qualitative Sub Study Results

All participants were asked at each follow-up whether they were willing to participate in the qualitative sub study, although at six months follow-up, those who had participated in the qualitative sub study at three months were not asked again. Of those invited, no participants refused outright to take part in the qualitative sub study, and of those who took part no one dropped out or withdrew. However an interview was stopped early by the researcher due to a participant becoming upset when describing the reason for their relapse. Figure 2 shows recruitment into the qualitative sub study.

****Figure 2. Qualitative sub study flow diagram RP trial****



UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Qualitative research participants were divided fairly equally across the trial arms, although fewer (17% of qualitative research participants) were from the S3P only arm. Around half (51%, 48/94) of the qualitative subjects were abstinent smokers; just over a quarter (27%, 25/94) lapsers, and just under a quarter (22%, 21/94) had relapsed.

## Participant characteristics

Table 21 gives the characteristics of the qualitative sample across the trial arms. About sixty per cent were from Australia, just over half (55%) were female, and 30% were between 51 and 60 years old. Just over a third had completed secondary education only, 54% were not working and 60% were in receipt of benefits.

Table 21. Characteristics of qualitative sub study participants

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Total**  **N=94** | **Usual Care**  **N=24** | **NIC**  **N=27** | **S3P**  **N=16** | **NIC+S3P**  **N=27** |
| **Country, N (%):**  **Australia**  **England** | 56 (59.6)  38 (40.4) | 18 (75.0)  6 (25.0) | 14 (51.9)  13 (48.1) | 10 (62.5)  6 (37.5) | 14 (51.9)  13 (48.1) |
| **Sex, N (%):**  **Male**  **Female** | 42 (44.7)  52 (55.3) | 10 (41.7)  14 (58.3) | 14 (51.9)  13 (48.1) | 9 (56.3)  7 (43.7) | 9 (33.3)  18 (66.7) |
| **Age, years, N (%):**  **18-30**  **31-40**  **41-50**  **51-60**  **61-70+** | 19 (20.2)  20 (21.3)  18 (19.1)  28 (29.8)  9 (9.6) | 3 (12.5)  7 (29.2)  5 (20.8)  7 (29.2)  2 (8.3) | 5 (18,5)  4 (14.8)  7 (25.9)  10 (37.0)  1 (3.7) | 4 (25.0)  3 (18.7)  2 (12.5)  5 (31.3)  2 (12.5) | 7 (25.9)  6 (22.2)  4 (14.8)  6 (22.2)  4 (14.8) |
| **Level of Education, N (%):**  **Primary School**  **Some Secondary**  **Completed Secondary**  **Some Tertiary**  **Completed Tertiary**  **Further Education/Diploma**  **Higher Education**  **Does not wish to answer** | 3 (3.2)  4 (4.3)  33 (35.1)  18 (19.1)  16 (17.0)  9 (9.6)  8 (8.5)  3 (3.2) | 0 (0)  3 (12.5)  6 (25.0)  6 (25.0)  4 (16.7)  2 (8.3)  1 (4.2)  2 (8.3) | 1 (3.7)  1 (3.7)  13 (48.1)  3 (11.1)  4 (14.8)  2 (7.4)  2 (7.4)  1 (3.7) | 1 (6.25)  0 (0)  4 (25.0)  4 (25.0)  4 (25.0)  1 (6.25)  2 (12.5)  0 (0) | 1 (3.7)  0 (0)  10 (37.0)  5 (18.5)  4 (14.8)  4 (14.8)  3 (11.1)  0 (0) |
| **Employment Status, N (%):**  **Working Full Time**  **Working Part Time**  **Neither** | 24 (25.5)  19 (20.2)  51 (54.3) | 5 (20.8)  6 (25.0)  13 (54.2) | 9 (33.3)  3 (11.1)  15 (55.6) | 3 (18.8)  5 (31.2)  8 (50.0) | 7 (25.9)  5 (18.5)  15 (55.5) |
| **Receiving Benefits** | 56 (59.6) | 17 (70.8) | 17 (62.9) | 11 (68.8) | 11 (40.7) |

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

In the following sections when giving illustrative quotes, we list: whether participants were abstinent, lapsed or relapsed (according to the definitions given earlier); trial arm; whether interviewed at the three or six month follow up (FU); gender; age in years; country.

## Summary of key findings

Analysis identified the following themes (see emboldened phrases) as most persistent across participants’ accounts:

(1) **Adversity in participants’ lives** which were interweaved with their smoking and relapse experiences;

(2) Many reported using **multiple study and non-study relapse prevention strategies** to cope with urges to smoke, there was differential engagement with study interventions and additional benefit was derived for some from **the study surveys and the EMA sub study** (where appropriate).

(3) The **acceptability, use and impact of study interventions** varied across study arms, for example in relation to the NIC arms, the products offered had different perceived strengths and weaknesses, there were concerns around e-cigarette safety, particularly in Australia, and there was a desire to taper nicotine content over time; the S3P advice and strategies were useful when accessed, but difficulties with access were commonly reported and a preference was expressed for an easier method of use, specifically a mobile phone app rather than a web-based programme; texts were a helpful reinforcement and could be improved if their content and timing were tailored to individual circumstances, but there were some reports that texts triggered urges to smoke.

(4) **The battle to overcome craving** played a key role in relapse, and

(5) **Differential responses to lapses and relapse**

It should be noted that the trial was complex, involving a number of different processes including baseline/three month/six month surveys, differential text messages according to study arm and user interactions, choice of product in the NIC arm and the option to switch product if desired, postal delivery of product/leaflet, one week follow up call (IV arms), option for further supplies if desired, prompts to use the S3P which varied according to their assessment responses online, and the EMA sub study. Additionally, some participants continued to use their base medications (those used in their quit attempt e.g. varenicline and nicotine patches) during the study period. Furthermore, especially when the inclusion criteria were extended in Australia to include one-week quitters, there was potential for the participants to confuse elements of any support they had received for their quit attempt with the relapse prevention interventions. Some participants struggled to distinguish the research elements (such as the surveys and EMA sub study) from the study interventions, and at times to disentangle their acute cessation treatment from the relapse prevention interventions. These reported instances should be borne in mind when reading further.

## (1) Adversity in participants’ lives

A very strong theme running through the majority of the interviews which provided an important context, were the difficult circumstances of participants’ lives. Many discussed lapses or relapses in the context of people close to them dying, of diseases (often smoking related) but on occasion also suicides, participants’ mental health issues (such as depression, bipolar disorder etc.), and their use of smoking to combat loneliness, stigma, and blame. On occasions they referred to relationship problems such as divorce. Frequently participants referred to their own physical health with descriptions of smoking related diseases such as heart and vascular disease and lung disease, and on a few occasions struggling with abstaining from other substances such as alcohol or marijuana. Many had been smoking for a long time, sometimes at very high daily cigarette consumption.

*“I was smoking eighty ciggies a day, look where I am a year later I’m on five or six*” [Relapsed/S3P/6 Month FU/Female/51years/England].

Or they reported having been trying to quit for a long time ‘*it’s twenty-five years I’ve been trying to quit’* and talked about how they had lost periods of their lives due to smoking.

*“I’ve lost fifteen years to smoking”* [Abstinent/NIC+S3P/3 Month FU/Female/31 years/Australia].

## (2) Multiple Study and Non-Study Relapse Prevention Strategies

The majority of participants reported using different motivational, behavioural and pharmacological strategies, for different situations and at different time points in the study period.

*“The vaporiser was useful for that earlier part and the nicabates now I find are pretty useful”*’ [Abstinent/NIC+S3P/3 Month FU/Female/59 years/Australia].

Some tools were study interventions, others were non-study methods, and many participants used a combination of strategies, including both study and non-study methods simultaneously. It was commonly recognised that that different strategies are likely to work for different people.

“*What works for one mightn’t work for another”* [Abstinent/NIC/6 month FU/Male/62 years/Australia].

*“Not everyone fits the same mould obviously I know that but erm there’s not a one thing fits all you know, their approach to their recovery is different and different things will work obviously, I can’t say one thing works even for me type-thing, you know I can’t say anything constructive on that really, I’m still learning myself”* [Relapsed/UC/6 Month FU/Female/33 years/Australia].

In terms of motivational strategies for relapse prevention, participants drew attention to the importance of having a clear understanding of their reasons for quitting, planning in advance and setting goals, self-positioning as a non-smoker or ex-smoker and having a strong sense of willpower, commitment and determination. Willpower was frequently perceived as the most important element, regardless of support strategies.

*“And I don’t think anybody’s in a position to, the support is great but I don’t think you can, I don’t think one can stop for anybody, if that makes sense, it’s a personal thing”* [Abstinent/NIC/3 Month FU/Male/57 years/England].

In relation to behavioural strategies, the importance of rewarding oneself for abstinence, changing routines e.g. tidying up, going shopping or not drinking coffee in the morning or at all, were highlighted. Distraction as a strategy was commonly reported in the form of walks, going to the gym, keeping busy, drinking water, using non-nicotine containing gum and mints, breathing techniques; and meditation was noted by a few as helpful.

*“Like every morning that was my favourite cigarette, that was the one I enjoyed, the rest of them during the day were just habit, nicotine addiction, but the only one that I really really enjoyed was my first one with my cup of coffee so now I don’t have my cup of coffee first thing when I wake up I wait”* [Abstinent/NIC/3 Month FU/Male/54y/England].

Some mentioned noting down urges and feelings such as stress in a booklet, or recording days quit and money saved on a calendar. Some used the strategy of confronting risky situations for relapse (e.g. socialising with alcohol) whereas others felt it was important to avoid such situations, particularly at the beginning of quitting. Indeed, reducing alcohol consumption, or stopping altogether, was mentioned by some as crucial to them staying quit.

*“Originally I didn’t go out to places where smoking or alcohol was going to be”* [Relapsed/NIC+S3P/6 Month FU/Male/62y/Australia].

Smoke-free environments and a sense of social stigma toward smoking were mentioned as important elements in staying quit.

Several participants were still using non-study medications such as nicotine patches or Champix when they joined, which they carried on using throughout the study period sometimes in addition to the study interventions, and which were reportedly helpful.

*“I just went on the Champix and it blocks your cravings and I found that a lot better, [..] and I have your e-cig and the e-ciggie is always there in case you do fall, and I think that’s a good idea”* [Abstinent/NIC+S3P/3 Month FU/Female/47 years/England].

*“I had the lozenges as part of my support from the doctors, NHS quit smoking service, she gave me loads of those so I’ve had them left over”* [Lapsed/NIC+S3P/3 Month FU/Male/29 years/England].

A sense of feeling supported was highlighted as important in staying quit.

*“That positive feeling you know that they’re with you and they want you to succeed*” [Abstinent/NIC&S3P/6 Month FU/Female/61 years/Australia].

For example, the role of social support from partners, family and friends (or for some a lack of support) was highlighted by many as an important motivation to maintaining abstinence. For some this was having people close to them who were quitting at the same time, for others just people to offer support when needed.

*“But addiction is pretty strong, so you need to have a wing man that can be very strict with you if they need to, someone that you really trust”* [Lapsed/S3P/6 Month FU/Female/35 years/Australia].

Others discussed more structured support from their GP, quitlines and mobile telephone apps as being helpful in addition to, or instead of, the study interventions.

*“They gave me what they called an emotional backpack*” [Abstinent/UC/3 Month FU/Female/39 years/Australia].

*“I’ve been using an app since I stopped smoking it’s not the NHS one because I didn’t like the NHS one it’s another one called QuitNow which I found really motivating and I still do when I look at it I can see how many days it’s been since I stopped smoking and how many cigarettes I’ve avoided and how much lunch money I’ve saved erm yeah so that’s sort of enough of a motivation rather than having those text messages”* [Abstinent/NIC/3 Month FU/Female/46 years/England].

For several participants, it was difficult to distinguish between all the methods that they had used, and state definitely which single strategy worked for them

“*It’s not just one of them, it’s all of them”* [Abstinent/S3P/3 Month FU/Female/37 years/England].

The strategies used were part of an ‘*overall package*’ or a ‘*concerted effort*’ to make use of all the tools available to them, without which many of those who were abstinent imagined they might have relapsed.

*“The texts, the QuitCoach and the nicotine substitute or in my case I had the e-cigarette down to no nicotine erm but it was just the comforting fact that I’ve spent thirty years with a cigarette in my hand and now I have something else in my hand so that is the whole package…I think if someone tried to give up or tried an e-cigarette or that Nicabate or whatever it is erm without other support I don’t think that it’d work”* [Abstinent/NIC+S3P/6 Month FU/Male/62 years/Australia].

***Surveys***

Some participants perceived the screening, baseline and follow-up surveys as an intervention in themselves, or at least partly, suggesting a possible ‘Hawthorne’ or screening effect 29.

*“I think maybe the survey a bit sooner might’ve helped me too* […] *If I had the survey at maybe six week intervals to start with”* [Lapsed/NIC/3 Month FU/Female/60 years/Australia].

Others referred to completion of the surveys as part of the bundle of interventions without which they imagined they would not have been able to stay quit, and that providing responses to the survey served as

“*more of a reminder to keep giving up*” [Abstinent/NIC&S3P/6 Month FU/Male/62 years/Australia].

***Sub Study: Ecological Momentary Assessment***

Although we did not specifically ask about the EMA sub study, some participants spontaneously mentioned the device during the interview. Like the surveys, many participants perceived the EMA sub study to be an intervention rather than a data collection tool. The device was described as helping participants realise what their triggers were by asking questions about thoughts of smoking or temptations in certain situations. It helped them to identify feelings related to the temptation to smoke, and to identify how urges might be related to certain situations, specific times and places, which they could then change or avoid.

*“It made me realise what things were triggering me off erm because it would say well have you had a thought about having a smoke within that time or were you tempted and I would say actually yeah I was and then I’d think back to when, when did I feel tempted and why did I feel tempted and I think that helped it to actually erm realise what things to avoid”* [Lapsed/UC/3 Month FU/Female/38 years/Australia].

*“The questionnaire with the handheld device you know with the phone thingy, and that helped as well* […] *It’s in your mind not to smoke because you’re taking part in that and that’s another reason not to do it because it kind of switches your mind away from it so that’s helped as well”* [Abstinent/NIC/3 Months FU/Male/51 years/England].

Some also suggested that having to add lapses to the device acted as a deterrent to smoking. Some participants partly attributed their ability to stay quit to the EMA as follows:

*[Researcher: And what do you think lies behind success?] “A good support base so that’s from my advisor my partner, and obviously the motivation with the EMA I’m doing as well”* [Abstinent/NIC+S3P/3 Month FU/Male/25 years/England].

*“I became dependent on it actually I kind of looked at it as I didn’t want to have to put relapse on it I didn’t want to you know disappoint this electronic thing”* [Lapsed/UC/3 Month FU/Female/38 years/Australia].

However, others referred to how after the initial benefits of using the EMA, the device then had served as a constant reminder that they could not smoke which subsequently initiated intense cravings. These, however, returned to ‘normal’ after the device was returned.

## (3) Acceptability, use and impact of study interventions

In this section we discuss feasibility, acceptability, barriers and facilitators of the interventions in the different arms of the trial. For the combined arm (NIC+S3P) we discuss any synergistic or other effects of having both interventions: comments on the individual interventions are discussed within the specific intervention sections (NIC or S3P). As text messages were sent in all arms these are discussed separately, including the enhanced messages alongside the S3P.

***Usual care arm***

A minority mentioned not relying on any specific strategy other than contact with the study team and the study texts and some even mentioned explicitly that they were against any other type of support.

“*I’m anti that type of thing I’m a person where I just do everything on my own terms so I’ve not used anything”* [Usual Care/Abstinent/3 Month FU/Female/39 years/Australia].

A few reported how they would have appreciated the opportunity to have selected study products but did not have the opportunity as they were allocated to the control arm of the trial.

*“Well personally when the choice was made at the start, I would’ve preferred to have been on the inhalers, because I’ve been on them before and they’re what helped me give up a couple of years ago, and I didn’t have the chance for that this time, so giving up this time wasn’t as successful”* [Relapsed/UC/3 Month FU/Male/48 years/Australia].

As discussed above, however, many participants in the Usual Care arm reported using a range of behavioural, pharmacological and motivational strategies to stay quit.

*“I got it [e-cigarette] about the same time I started the programme, yeah it’s been over three months*. *I’m going to get the patches the nicotine patches and I use the inhalator, is that what it’s called, what you put the cartridge in, I use that as well, and I try to stay away from alcohol as well”* [Relapsed/UC/3 Months FU/Female/40 years/England].

*“A mixture of things, some of it was like in Victoria we have like a helpline to quit smoking, some of it was using a vape pen, that was good too, and some of it was, I don’t know motivation because I have a young daughter now so I had a bit more motivation to quit now than I had before”* [Abstinent/UC/3 Month FU/Male/34 years/Australia].

***Nicotine product arms***

* ***Product choice: acceptability***

The process of choosing a suitable product was explored. Some participants talked about how they had tried several products during previous quit attempts and had developed a sense of which products had *‘not worked’* for them (such as taste or side-effects) which had informed their choice of study product.

*“I had the patches before and they made me really ill, yeah they didn’t agree with me, but I think the spray’s really good”* [Abstinent/NIC/3 Month FU/Male/46 years/England].

There had been a lot more prior experience with different nicotine replacement products, so often an e-cigarette was chosen because it was the most novel product on offer.

*“The other options I’d already tried and they had not worked*” [Abstinent/NIC+S3P/3 Months FU/25 years/England].

Others talked about trying one product then switching to another one because it was not suitable. Many described ‘*trying*’ and ‘*finding*’ different products until an acceptable strategy was found.

*“Just to try different things for me, I tried everything else and I had the chewing gums you know from the stop smoking service, the chewies you know I thought were OK, they did help me, and I thought I’ll try the minis and they were helpful, and then I thought I’d try the spray since it’s being offered like, I’m really happy with the spray, it does help a lot”* [Abstinent/NIC/3 Month FU/Male/54 years/England].

Palatability of products was a key criterion, particularly for NRT products, and this differed across participants with the same product being unacceptable to some and the preferred option for others, again emphasising the fact that there is no ‘*one size fits all’* solution. For example, some mentioned the taste of the spray as repulsive, particularly with alcohol, although for others using the spray when drinking alcohol was acceptable. The mint taste of the lozenges was disliked by a few ‘*I’m not a minty person*’ or ‘*vile*’ and ‘*nasty*’ whereas others described the taste as acceptable, ‘*more palatable*’, or ‘*quite refreshing*’ as one participant put it. The flavours of the study e-cigarette (tobacco and menthol) were broadly acceptable; however, several commented that a wider range of flavours would be preferred. For example, some participants disliked the taste of the tobacco flavour as they had not smoked for five weeks and did not want to be reminded of the taste of tobacco. A few others, however, reported a preference for tobacco flavoured e-liquid. Others bought their preferred flavour separately and added it to the study e-cigarette. However, it was acknowledged that tobacco cigarettes do not taste very nice either. The barrel of the e-cigarette was described as too small for those who used the e-cigarette frequently, and there were some concerns expressed about the e-cigarette unexpectedly running out of battery charge.

Some described physical reactions particularly to the spray and lozenges, such as hiccups, heartburn and a sore throat which deterred them from using or led them to try other products. Physical reactions or oral surgery sometimes had led some participants to try vaping. Others described these factors as *‘not being able to tolerate’* or ‘*just didn’t get on with it’* or physically not being able to use the products correctly which ruled them out.

*“They told me the options then I said OK I’ll try the spray but I couldn’t open my mouth wide enough to spray it onto the inside of my cheek, I kept getting it on my lips, it was unpleasant and it was not something that I’d look forward to doing so I didn’t use that”* [Abstinent/NIC+S3P/3 Month FU/Female/69 years/England].

Speed of action and strength were other important factors influencing their choice of NRT product and these product characteristics often seemed inter-related. For example, the effects of the spray were described as ‘*fast’* and giving ‘*a very immediate hit of nicotine*’ which was good for some but for others was ‘*too intense*’, ‘*aggressive*’ and ‘*compulsive*’ for the same reasons. A participant described the nicotine patches received from their GP as ‘*not very much help*’ as they only provided a ‘*maintenance dose*’ of nicotine. This was unacceptable to this participant as they wanted to be able to ‘*alter the frequency or the strength of the stuff* [nicotine]’ and for this reason had selected the spray, for ‘*more immediacy and control basically*’. Many alluded to a need to ‘*control*’ nicotine intake but views differed on which products facilitated better control, with some believing the slower release of nicotine through products such as lozenges was more ‘*controllable*’ and ‘*more easy to control*’ than the spray. E-cigarettes simulated smoking in certain ways for some users, but reportedly they did not give the same ‘*kick*’ or ‘*hit*’ as smoking which in a few cases led to overuse.

*“I was smoking more the e-cigarette than a cigarette constantly, because I wasn’t getting that hit”* [Relapsed/UC/6 Month FU/Male/50 years/England].

For others, the throat-hit was key and reportedly *‘missing’* from the spray. Occasionally, the throat hit was too strong reportedly burning the back of the throat. Sometimes negative characteristics such as this were perceived as being helpful but deterred sustained use, for example:

*“You’re not as encouraged to use it [spray] because of the crazy taste that it leaves in your mouth for so long* […]*and I know the concept of it is not to make it so desirable so you’re replacing smoking with anything else, but eventually the desire is to not have it”* [Lapsed/NIC+S3P/3 Month FU/Male/29 years/England].

Price was another factor. For example, e-cigarettes had been too expensive for some participants to buy for themselves and therefore they selected it as part of the study, viewing these as really valuable. Price was also a factor in selection of (and continuing to use) NRT products. For others the comparable price to cigarette smoking led them to lapse.

*“Oh I can’t be bothered to keep buying these they’re the same price anyway so I might as well have a cigarette and do something that I enjoy”* [Lapsed/NIC/6 Month FU/Female/23 years/England].

Some participants appreciated how the lozenges were discrete and very different from smoking as they lasted longer or were minimally disruptive (e.g. not having to go outside).

*“It wouldn’t interrupt what I was doing”* [Abstinent/NIC&S3P/3 Month FU/Female/33 years/England].

In some cases the NRT product was chosen as it prevented smoking, for example by putting a tablet or gum in the mouth, one then could not smoke. A few participants could comprehensively list all the pros and cons of different products they had tried or used underscoring the extent to which smokers will go to understand and get the right type of support. Some described how they did not want to use products such as an e-cigarette because they were reproducing or ‘*emulating’* the hand-to-mouth actions associated with smoking and for others this was precisely the reason why they preferred such products. In the latter category, participants often regarded e-cigarettes as very similar to smoking but a ‘*cleaner’* way to consume nicotine compared to smoking, whereas others stated that they had expected the e-cigarette to be similar to smoking only to find the effects were not the same. In some cases it was acceptable if vaping wasn’t exactly the same as smoking as they had not sought to completely replicate the tobacco cigarette smoking experience.

*“It’s not like a cigarette where you have a cigarette and you smoke a cigarette, with the e-cigarette you have one or two puffs, it’s completely different from smoking”* [Abstinent/NIC+S3P/3 Month FU/Male/51 years/England].

One attractive characteristic of products was the ability to reduce nicotine intake ‘*to wean down that dose’* over time; this could be done by e.g. reducing the number of lozenges taken, but more commonly this was noted in relation to e-cigarette use. Common to both countries were buying non-study nicotine separately and ‘*diluting*’ or overtime gradually reducing the amount of nicotine in the e-cigarette liquid to zero. The e-cigarette could most easily be tailored to individual needs, both by varying nicotine content as well as the use of different flavours. For example, one participant described it as:

*“One of the greatest tools [...] start diluting the nicotine and change the flavours and gradually cut down yourself”* [Relapsed/NIC+S3P/3 Month FU/Female/56 years/Australia].

* ***Rejection of all NIC products***

There were concerns about the long-term health risks of vaping *in five years’ time find out oh s\*\*t it actually was worse than smoking’.* One participant assumed that as the products were given to them by the study team that they were not harmful.

*“Because I was really worried that it would be [harmful], that that it is actually doing my lungs harm, I’m assuming it’s not”* [Abstinent/NIC/3 Months/Female/54 years/Australia]*.*

Worries emanated largely, but not exclusively, from participants in Australia . A few, again predominantly from Australia, felt that the research team could have provided detailed literature on the safety and risks of e-cigarettes, which would have helped them to decide on whether or not to use that product, particularly for first-time use:

*“If you give me like a brochure that says like this is the effects this is the risks these are the risks of doing this compared to the risks of smoking which is obviously like backed by research and whatever and then compared to none, compared to nothing compared to fresh air and then also compared to walking in the city […] all those things should be clear for me to make a decision on a product that I’m willing to take”* [Lapsed/NIC+S3P/3 Month FU/Male/24 years/Australia].

Some participants rejected all the study products on offer. One of the main concerns was that they did not feel they needed such support ‘*I’m an all or nothing person, you know I’m either smoking cigarettes or I’m not smoking*’ or that the support ‘*would just lead me back to smoking eventually’. Others* rejected the products because they did not want to become ‘*hooked*’ or dependent on something else ‘*developing another addiction after stopping smoking*’ [Abstinent/NIC/3 Month FU/Female/38 years/England] and this was mostly, but not exclusively, in relation to e-cigarettes. Common concerns included *‘substituting one addiction for another addiction’*, or ‘*replacing a harm with a harm*’. Another participant likened use of an e-cigarette as a tool to a ‘*vegetarian eating vegetarian sausages*’ which to them was ‘*pointless*’ as it was at odds with their idea of what it means to stay quit.

*“For me I prefer to work with the head stuff, for me I prefer to do the talking to myself stuff than substituting with things like that or substituting with an e-cigarette, I want to get rid of the habit I don’t want to substitute”* [Lapsed/NIC/6 Month FU/Female/60 years/Australia].

Other concerns raised were by those who had stopped all nicotine use when they were enrolled into the relapse prevention study and did not want to start using nicotine again, as they felt it increased the risk of relapse.

*“I’ve pushed myself to the ultimate limit and I’m trying not to use the liquid mist I was given by the prevention team because I don’t want to have the nicotine in my body anymore, because if I feel like I’ve got nicotine in my body I’m more likely to relapse than if I don’t take it* […] *I haven’t used it [Nicorette Mist] to be honest, it hasn’t been that bad, and because obviously I’m trying to keep nicotine out of my system I’ll only use it if I desperately need”* [Abstinent/NIC+S3P/3 Month FU/Male/25 years/England].

In a similar vein, many commented that offering nicotine-free e-cigarettes as a study option would have been beneficial. Some participants believed that a non-nicotine e-cigarette would help them to cope with any persistent behavioural habits related to smoking, such as providing the hand-to-mouth and exhalation of vapour actions, but without the nicotine.

*“So I got one [nicotine-free e-liquid], but I took the nicotine ones just as a back-up in case I ever do relapse, because if I did relapse, this is how I was thinking, if I had the oil-free ones if I’d been on nicotine it wouldn’t work, I’d have to go back to the nicotine one and reduce myself off it again, you know what I mean, but I was thinking that you could throw no-nicotine ones in as a choice for people who’ve been on Champix”* [Abstinent/NIC+S3P/3 Month FU/Female/47 years/England].

It was clear that there was widespread misunderstanding about nicotine for the purposes of relapse prevention.

*“Like it’s defeating the object really…when you’re doing the nicotine one it’s still like you’re smoking if you know what I mean because it’s still nicotine isn’t it”* [Abstinent/NIC+S3P/3 Month FU/Female/51 years/England]*.*

There was little understanding among the majority of the role of nicotine in helping people to stop smoking, instead perceiving that using nicotine again could *‘elevate’* the risk of relapsing to smoking. Among some, there was high resistance to its continued use. A few, however, clearly understood the role that the NIC products were meant to play in a quit smoking attempt, for example:

*“What really works for me is to try and separate out the chemical addiction from the actual behaviour of smoking yeah because that way you directly displace the smoking with just the, it’s almost like reducing down to the addiction let’s just deal with the addiction”* [Abstinent/NIC/3 Month FU/Male/59 years/England].

In addition to a wider range of flavours as discussed above, some participants mentioned that the study may have benefitted from offering a wider range of NRT products such as options for gum and patches. These participants perceived that the gum was more palatable than the spray and the chewing action element of the gum was viewed as:

“*partly a replacement for the ritualistic aspect of smoking*” [Abstinent/NIC/3 Month FU/Male/59 years/England].

* ***Use and Impact***

In line with the study advice, when the NIC products were used, mostly this was to help with urges to smoke so they ‘*don’t feel tempted to smoke’*. How they were used to achieve this, however, differed.

Some described more frequent and compulsive use throughout the day in a planned way to maintain nicotine levels and reduce cravings occurring *‘I give myself two squirts [spray] every two hours’ or ‘I take one or two puffs [e-cigarette] once an hour’* [Abstinent/NIC/3 Month FU/Male/54 years/England]. These users either began use straight away, or only started the NIC when they came off their base cessation medications, for example:

*“I’ve only started using it the e-cigarette in the, in the last week of the three month period, I was using patches and I started using the e-cigarette just to get used to it and once I came off the patches I’ve been using it consistently and whenever I used to smoke I use the e-cigarette now”* [Abstinent/NIC/6 Month FU/Male/31 years/Australia].

For some e-cigarette users, there were concerns about transferring their dependence.

*“But now I’m just addicted to it, the e-cigarette, I don’t even think about cigarettes nowadays, it’s a nicotine thing”* [Lapsed/NIC+S3P/3 Month FU/Female/39 years/England]*.*

One participant was concerned that they would have to stop using their e-cigarette soon (because of visiting family members who would not like it) and were very concerned about how they would manage (anticipating failure).

Other participants talked about using the NIC product only in certain situations and only at certain times, such as at night, after meals, walking the dog, with alcohol, when stressed, and when socialising, mainly as these times were when urges to smoke were greatest. Some would use the product regularly in these situations ‘*I’d grab it (e-cigarette) and I’d go and have two big puffs outside and then I would just go back inside’*. Sometimes it would be used in anticipation of craving rather than waiting for the craving: ‘*about ten half ten I might start thinking oo I haven’t had a ciggie yet and that’s when I’ll get the spray’*. These participants stated that they needed several minutes for the nicotine to kick in.

*“If you can anticipate a craving and you need five or seven minutes for that to work”* [Lapsed/NIC/3 Month FU/Male/34 years/Australia].

Others, however, would carry around the NIC product all the time, but only to use it in vulnerable situations and only if they felt a great need. These participants were storing the NIC for *‘emergencies’,* without the intention of using but there as a *‘fall back’*, *‘safety net’*, or when ‘*desperate*’. These participants often placed greater faith in their motivational beliefs for stopping, drawing on ‘*mind over matter’*. For example, one participant mentioned that they knew it was good to have the NIC products available even if not using, but to ‘*feel more secure*’ as they were concerned as they had had nicotine in their ‘*system*’ for the past fifteen years and did not know when they might be overcome with urges. Use in social situations was commonly reported, sometimes as they did not want to be ‘*left out’* while others are smoking. Many reported a benefit of the e-cigarette was that it enabled them to continue to socialise with tobacco cigarette smokers. So, these participants did not avoid difficult situations which were enjoyable but embraced them by using their NIC product, for example:

*“I’ve got the second method as well which is the e-cigarette and that has been very helpful for the other situation which I was managing with the lozenges but erm, which is sort of easier to manage with the e-cigarette and that is I’ve got two friends who smoke so seeing them it’s easier if I have an e-cigarette because erm yeah I’m not tempted to ask them for a cigarette”* [Lapsed/NIC/3 Month FU/Female/57 years/Australia].

*“When I was in the situation where I did go out with my girlfriends and they were smoking I would grab a lozenge out of my bag and have that instead of the cigarettes”* [Abstinent/NIC+S3P/6 Month FU/Female/25 years/Australia].

It was clear that for some participants different NIC products were used for different reasons, purposes and situations. One participant talked about using the e-cigarette in social situations and nicotine gum (a non-study product) while at work in a bar where they were not permitted to use the e-cigarette.

In relation to impact, generally the different products worked well in combating and controlling craving ‘*killing the craving’*, and for some participants there didn’t appear to be a prior expectation that they would work.

*“And they did actually stop some of the cravings”* [Relapsed/NIC+S3P/6 Months/Male/43 years/England].

*“The spray is excellent it stops the craving almost immediately”* [Abstinent/NIC/3 Month FU/Male/54 years/England].

*“Without that I probably would’ve failed, that was there every time I had the urge I could go and reach for one of those little lozenges”* [Lapsed/NIC+S3P/3 Month FU/Female/48 years/England].

A combination of NIC products were sometimes reported to combat craving as well.

*“So I was already using patches and I found the lozenges just augmented it when I needed it […] I took the patch off at night time to sleep, and first thing in the morning I put a patch on and I put a lozenge in my mouth, it’s for an instant thing”* [Relapsed/NIC+S3P/6 Month/Female/69 years/Australia].

*“Yes I think from a scale of zero to ten the lozenges is like a six but the main thing is your own self-control and when you combine the lozenges and the e-cigarette it’s like eight yeah”* [Lapsed/NIC/3 Month FU/Male/34 years/Australia].

Of those who had lapsed, many talked about how they used the NIC products to help them get back to quitting and hence did not relapse fully. Others talked about how they relapsed when they stopped NIC use:

*“Then I thought to myself I can’t go on forever using this so I had to come off all kinds of nicotine, which I did, and I was able to get away from any kind of nicotine for a good few weeks”* [Relapsed/Usual Care/6 Month FU/Male/50 years/England].

For a few participants, the use of the products in some situations was associated with improved wellbeing or mental health, for example, being:

*“able to hang around with people while they were smoking and be social, it improved my mood to be honest”* [Abstinent/NIC/6 Months FU/Male/25 years/Australia]*.*

For others, it was the ability to have something to do with one’s hands and mouth that seemed to be the most important aspect.

*“Because in the past I’ve tried quitting but found it boring without using my hands, so because I’ve got used to my mouth being with a cigarette so I didn’t have that in the past and I’ve ended up relapsing, and the time with the e-cigarette it felt like I had something to do with my hands and something to inhale, yeah so that helps me but it’s not something that I intend to use permanently”* [Abstinent/S3P/3 Month FU/Female/37 years/England].

* ***Reducing nicotine***

As stated above, reducing nicotine intake was a common desire which for several participants was implemented somewhat regimentally:

*“I used the vaping method to reduce, so what I did was erm I started off with ten percent nicotine level then I’d say almost weekly or say fortnightly would reduce that, and within two months I was down to zero nicotine in the vape, erm and then I kept vaping for another two months, and I haven’t vaped for two months or so”* [Abstinent/NIC+S3P/6 Month FU/Male/62 years/Australia].

A few who had relapsed described how they liked using the e-cigarette but stopped using it following relapse. However, many who relapsed mentioned continuing to use the e-cigarette which they believed helped to reduce the amount they were smoking.

***S3P arm***

* ***Acceptability, barriers, facilitators***

The ability to access QuitCoach of their own accord was a benefit for some.

*“*I*t sort of gives you your own choice as to whether you want to* use *like you log-in or not log-in as much as you want”* [Lapsed/NIC+S3P/3 Month/Female/33 years/England].

However, this was also acknowledged as a barrier as they needed more reminders, prompts or persuasion to log in. It was even suggested that logging in a number of times in the first few weeks should be ‘*mandatory’* in order to get into the habit of using it. Some found having to log in to the study website as bothersome in terms of remembering their username and password every time they wanted to access QuitCoach, especially after not using it for a while. This deterred many participants from using it either once or, after the first access.

*“I can honestly say that* *I haven’t even been to it”*  [Relapsed/NIC+S3P/3 Month FU/Female/56 years/Australia].

*“I have to go into my emails find my username find my password then go into the website”* [Lapsed/NIC+S3P/3 Months FU/Male/24 years/Australia].

A few suggested that an ability to request a text with log-in details would have been beneficial, or simply being sent them with a reminder text to go on would have been helpful.

*“See I’m not a very tech savvy person”* [Lapsed/NIC+S3P/6 Months FU/Female/37 years/Australia]

*“I’m not into computers”* [Relapsed/NIC+S3P/3 Month FU/Female/56 years/Australia].

Other barriers were technical issues logging on or issues with internet connection (due to living somewhere remote, for instance). However, a few remarked that once their username and password was set then logging into QuitCoach:

*“wasn’t hard work*” [Abstinent/QuitCoach/3 Month FU/Female/37 years/England].

Some tried to access it on their phone and found it very clustered. To this end, many stated they would have preferred an app instead.

*“But if it was something like an app where maybe you can incorporate the texts into it and then it just becomes like an erm how do you say it like a pop-up kind of thing yeah a reminder or something and some distracting games because that’s one of the things that happens when you’re craving I’m guessing you need to distract your mind”* [Lapsed/NIC+S3P/3 Month FU/Male/24 years/Australia].

Others found QuitCoach to be ‘*mind-boggling*’, ‘*long-winded*’, with repetitive questions, ‘*asks the same question over and over again*’, that ‘*go on for a while*’ after initial use which had stopped them from returning to it. Some suggested it was too much of a ‘*commitment*’ to get QuitCoach going.

*“Investment to get it up and going, erm and I don’t know if I gained that much value”* [Lapsed/NIC+S3P/3 Month FU/Male/29 years/England].

For example, a parent with a young child mentioned appreciating the option to use QuitCoach but had little extra time to go through it given her child only slept for about 20 minutes at a time. Those who accessed QuitCoach minimally (i.e. once) talked about how they may have engaged more if the information provided was more ‘*bite-size’*. As mentioned above, a preference was expressed by many for an app, and suggested improvements included a better user interface and gamification for distraction from urges to smoke. Others described the design layout of the QuitCoach website as ‘*laid out well*’, whereas others remarked that the user interface could be improved.

Others commented that it was difficult to provide an accurate answer to some of the questions in the assessment because of the pre-specified responses available.

*“I wasn’t able to give a definitive answer and I had to just choose one because it didn’t match up with my thoughts”* [Abstinent/NIC+S3P/3 Month FU/Female/69 years/England].

A few felt they did not need to use the online intervention at the time as they were:

*“trying to do it without being online because I’m not online all the time, so I need to look at it in the real world, in the context of that rather than going onto a website*” [Relapsed/NIC+S3P/6 Month FU/Female/56years].

Other reasons for not using QuitCoach included: already using non-study mobile phone quitting apps with comparable functionality, lack of incentivisation to stick with it, not liking to read materials online and failure to capture attention.

*“I’m old school so I find it hard reading materials online”* [Lapsed/NIC+S3P/6 Month FU/Female/age unknown/Australia].

Some preferred to speak with someone face-to-face and therefore did not take up the opportunity to use QuitCoach. Others did not engage with QuitCoach because they viewed it as a ‘*robot*’ or ‘*algorithm*’ and could not replace human interaction with a health professional.

*“What I really need is to talk to a doctor and to get real medical advice and to like you know, talk face-to-face with someone that’s a professional, I kind of just palmed it off a little bit”* [Lapsed/NIC+S3P/3 Month FU/Male/25 years/Australia].

It was possible, as mentioned previously, that some participants were confusing the various study tools or interventions, such as the follow-up surveys, with QuitCoach. Additionally, many of those in the S3P arms did acknowledge the utility and helpfulness of the text messages, which were more tailored in the S3P arms (see below).

*“I never thought about it [QuitCoach] because I was busy reading the text messages”* [Abstinent/NIC /3 Month FU/Male/24 years/England].

* ***Use and impact***

Some participants, who had already abstained for some time, reported having minimal urges and did not feel a need to use the QuitCoach, or they were combating the urges with other tools. However, for some, having to learn and use behavioural strategies recommended by QuitCoach was taken as an indication that they were not coping.

On the whole, however, when participants did log on to QuitCoach it was described as ‘*helpful’*, *‘positive’* and ‘*clear and concise*’. QuitCoach reportedly provided ‘*good advice*’ that served to ‘*recap*’, ‘*reinforce*’, ‘*encourage*’ and ‘*remind*’ them to stay quit. For example, QuitCoach asked questions such as what plans were in place ‘*when something goes wrong*’, which helped participants to consider, and potentially prepare, for such scenarios. QuitCoach was perceived by some as providing ‘*emotional*’ support that could be accessed whenever neededwhich was not something that a NIC product or existing stop smoking services provided.

*“It’s like a friend or a sister, it’s really good*” [Abstinent/S3P/3 Month FU/Female/37 years/England].

How QuitCoach was used, like NIC products, again varied considerably. Some described how QuitCoach was particularly helpful at the beginning.

*“Particularly useful at the start when you sort of like struggling*” [Abstinent/S3P/6 Month FU/Male/21 years/Australia].

Some found the *'scientific content*' to be beneficial to motivation and even wanted more of it.

*“It really made you think at the start about all those triggers and how your individual habit works, and how the addiction is in your individual life […] that mixture of scientific information about what was happening in my body and my brain together with yeah having a bit of a motivational kind of boost was really beneficial to have that together”* [Lapsed/S3P/6 Month FU/Female/35 years/Australia].

Some did not feel a need to return to it after the first use.

*“There’s things that I might not have thought of before that now I’ve got in my head already… that it makes you consider these things in advance”* [Abstinent/NIC+S3P/3 Month FU/Female/33 years/England].

Others used QuitCoach only when experiencing urges or for anticipation of urges and how to combat them*.* Some actively used QuitCoach online when they had strong urges to smoke.

*“And if I ever have one of the urges which are unbearable and I can go to the QuitCoach and fill in an assessment if I feel I can’t handle the urge and see what I can do to combat the urge”* [Abstinent/NIC+S3P/3 Month FU/Male/25 years/England].

QuitCoach generated a personalised report based on the assessment responses, which some participants repeatedly used for reference by either printing out materials or screenshotting advice for reference when needed ‘*I can reread it’*. The personalised advice was found to be helpful in terms of identifying and planning for situations that participants themselves had not identified, ‘*point out things that people might not be aware of*.’ It helped to identify ‘*things to watch out fo*r’ and ‘*times and places*’ at which they felt themselves most vulnerable to relapse (e.g. drinking alcohol or stress). QuitCoach helped to plan for such situations with something written down and therefore ‘*referenceable*’ and ‘*concrete*’. Participants who read their personalised advice liked how ‘*in-depth*’ it was, in particular the ‘*accuracy*’, with comments such as that it was the ‘*best advice*’ they had received to date or:

*“it knows how you think, it’s so intelligent’*. *It made me think of situations that might bother me before I’m stood in them you know so yeah it was definitely a helpful tool even if you don’t look at it again after you’ve filled it in, it’s the fact that it makes you consider these things in advance”* [Abstinent/NIC+S3P/3 Month FU/Female/33 years/England].

*“Do you know the beginning when you have to do this huge questionnaire and it gives you sort of like an elaborate step by step plan for you that was awesome, that was the best advice I ever got* […] *it had the tools it tells look you could be doing this you could doing a list you could do this do that, it was all tailored for me you know based on the answers that I gave and I thought that was very very useful”* [Abstinent//NIC+S3P/3 Month/Female/48 years/England].

The tailored advice, and the ability to update this advice subsequently when circumstances changed, was valued as ‘*really good*’, as a participant observed.

*“It altered it to fit the changes that had gone on*” [Abstinent/NIC+S3P/3 Month FU/Female/33 years/England].

QuitCoach was therefore helpful for participants to track their progression.

*“Just going back to it I was able to see how much has changed and* […] *maybe it gave me a sense of like developmen*t*”* [Abstinent/S3P/6 Month FU/Male/21 years/Australia].

Similar to NIC products, others described an intention to use QuitCoach only in an emergency situation, if *‘desperate’* or if the urges to smoke were ‘*unbearable*’, so that they could seek advice on how to ‘*combat the urge*’. These participants acknowledged that it was useful to know that QuitCoach was there if they ever needed it.

Strengths of QuitCoach included that it was interactive, not too formal, that it could be used as a distraction from urges to smoke, and that it was accompanied by tailored text messages (see next section).

For some, QuitCoach had been an adjunct used in conjunction with non-study strategies, while others reported using nicotine products such as the e-cigarette with and without regular use of QuitCoach.

***NIC+S3P arm***

Many of the views expressed in the combined arm about the individual products (NIC or S3P) mirrored those in the single product arms and therefore will not be repeated here. Instead, we focus on comments about the synergy between the NIC and S3P interventions.

Participants varied in the extent to which they used the two interventions, with some predominantly using NIC, relying more on the study NIC product alongside the tailored texts with minimal access to the QuitCoach aspect of the S3P intervention. Others predominantly used the QuitCoach, frequently due to their beliefs about nicotine and substituting smoking with NRT or an e-cigarette. Where participants made use of a NIC product alongside regular use of QuitCoach, they generally reported using the NIC product to prevent urges from occurring or to go to in an emergency to avert a lapse turning into a full relapse. QuitCoach appeared to help guide one participant in this situation.

*“But I think the QuitCoach yeah when I had a temptation to smoke when I was on holiday, and I had the e-cigarette”* [Lapsed/NIC+S3P/3 Month FU/Female/39 years/England].

Some participants acknowledged that QuitCoach alone could not ‘*override*’ physical urges to smoke which they felt the NIC product could help with, as it ‘*softens the edges*’.

*“They were both helpful and even the e-cigarette although with the QuitCoach it gives you things to watch out for and with the e-cigarette that’s my go-to let’s say I’ve had a bad day at work I’ll pick the e-cigarette over buying a packet of cigarettes, that’s pretty helpful because erm because if I bought cigarettes god knows what would happen, and an e-cigarette will do what it needs to in the case of an emergency sort of thing”* [Relapsed/NIC+S3P/6 Month FU/Male/33 years/Australia].

***Study text messages (all arms)***

* ***Non-Tailored and Non-Interactive Texts in (i) Usual Care and (ii) NIC only arm***

There were mixed views on the helpfulness of the standard stream of text messages for those in the usual care and NIC only arms of the trial, ranging from encouragement, reinforcement to stay quit (not necessarily the content, just the fact that the text messages kept coming in), through to annoyance to triggering thoughts and urges to smoke when they weren’t thinking about cigarettes. Some expressed a ‘*neutral*’ stance toward the texts or mixed views (e.g. *‘sixty per cent very good’*) with some text messages being helpful (either at some times of the day or on some days) and yet other texts (or on other days) could be less motivating.

Some reported the texts helped them to cope with urges, describing them as ‘*positive*’, ‘*extremely helpful*’, ‘*right kind of tone*’, a ‘*wake-up call*’, ‘*brilliant*’, ‘*an invisible friend*’, ‘*a pat on the back*’ and a ‘*back-up*’. Some noted that this was very different from the lack of support from family members who did not expect them to succeed in quitting for so long. This participant reported how the text messages had prevented a lapse going into a full-blown relapse on this occasion:

*“I’ve stopped for months and months and I’ve had a go and thought oh this won’t hurt me and then it does, it’s very easy to fall back into it but I found this time with the messages I’ve been getting, I’ve been getting text messages which I think are now down to about once a week, and I just found reflecting on those really helpful to get it into my head”* [Lapsed/NIC/6 Month FU/Female/60 years/Australia].

Conversely, others reported that the texts triggered urges or reminded them of smoking, ‘*the texts make me think of a cigarette*’ and *‘made the cravings worse’*. If they were not tailored then for participants who had relapsed, text messages that were encouraging people to stay quit were unhelpful and inappropriate.

Others remarked that the texts were only helpful at the beginning but then became monotonous, while some mentioned that they stopped reading the texts following relapse to smoking as they kept reminding them:

*“how bad I am for smoking again”* [Relapsed/NIC/3 Month FU/Female/33 years/Australia].

Many responded that they would like the text messages to be tailored to their own circumstances, such as timing and content or in relation to their own needs or circumstances or other forms of support.

Responses to the timing of the text messages varied. For example, some appreciated the text first thing in the morning to remind them not to have a cigarette and keep strong *(‘it just starts your day off in a positive way’*), others found them annoying as they would remind them of smoking.

*“Would remind me first thing in the morning because I’d be waking up and it’d already be on my phone and that would be the first thing I see when I wake up in the morning, going I’m trying to quit cigarettes and this is right in my face”* [Abstinent/NIC+S3P/3 Month FU/Female/31 years/Australia].

Some felt the frequency was just right and when they started to reduce the frequency they reported ‘*missing them*’. Others felt that the frequency of the text messages was right initially but should have been reduced more quickly. Participants would have liked to receive texts at times when they themselves experienced urges to smoke, such as scheduled breaks at work, mornings, and after food or for those on shifts for when they were awake. This would be possible if participants were asked when their urges were greatest or how frequently they would prefer to receive the messages. Others just wanted to see the timings of the text messages vary *(‘ad hoc’*) rather than always coming in at the same time of day.

The scientific content of the text messages, such as the health benefits, was well received, and many would like to have seen more of these, particularly those explaining how their body, e.g. their lungs, would have improved after abstaining for different lengths of time.

*“I wanted information about the body what’s happening in my body in the first you know twenty-four hours the first day second day and I wanted all the nitty-gritty about the body and what’s going on but I didn’t get that […] actually give me like little facts about erm like you know where is it if I can look at my actual tobacco the actual facts of the tobacco you know like the packet it’s got you know this BDE in capitals is found in large amounts of tobacco smoke you know and just erm but how my body is responding in recovery you know when I stop smoking like your hair your skin your organs what’s going on with your organs and giving me hope I needed to hear I needed to hear hope for the future with that like I’m scared I mean honestly I’m scared I’m going to have lung cancer you know”* [Relapsed/UC/3 Month FU/Female/47 years/Australia].

Another participant described how they did not socialise in bars and therefore the texts relating to coping in those situations had not been relevant. Some participants appreciated the text messages on the amount of money they were saving by staying quit, but others found these annoying, having succeeded several times at stopping smoking previously for periods of time, so they already knew all the reasons why they were stopping. Other participants wanted the texts to relate to the support they were using. That is, those not using NIC products were unhappy with texts encouraging them to using NRT or e-cigarettes when in vulnerable social situations as they were irrelevant (they also thought people using would not need encouragement to use them). They instead preferred more motivational messages on the positives of not being a smoker or negatives of being a smoker.

*“So maybe that’s what these constant texts is giving you, it’s reminding you of the good things and not the bad things, because when you stop smoking, for me it’s all about what I’m missing out on […] so those texts give me a or gave me or continue to give me that someone cares, someone yeah knows what I’m going through, or something, does that make sense”* [Abstinent/NIC/3 Month FU/Female/54 years].

Reasons for stopping the texts included that they were lost among the hundreds of other text messages they received in a day and instead feeling that they needed to speak to someone. A minority reported them to be ‘*worthless*’, ‘*irrelevant,* ‘*a bit too much*’, or ‘*over the top*’. Suggestions for improvement were also to make them interactive.

*“I pretty much ignored a lot of them […] I think the only way it might work is if people had the option to actually send a message when they felt like it and then get one back telling them not to do it”* [Abstinent/ NIC/6 Month FU/Female/44 years/Australia].

Participants described scrolling through texts as and when needed.

* ***Tailored and Interactive Texts from S3P and NIC+S3P Arms***

Varied views on the tailored and interactive text messages as part of the S3P arms were also apparent. Many suggested the tailored texts were ‘*reassuring*’, ‘*reinforcing*’, ‘*brilliant*’ and made ‘*good points*’ about which ‘*strategies*’ to use in different situations. Others remarked how the text messages received in the morning helped them to prepare for or become ‘*more mindful*’ of how they were going to ‘*deal with the day*’. Whilst ‘*impersonal*’, some described how the texts helped them to remember what they had accomplished in managing to stay quit, which had been a ‘*good feeling*’, and the ‘*recognition*’ had also been appreciated. Having the texts on a mobile phone to refer to whenever needed, for example when struggling during an urge, was also helpful for many. The tailored texts were described as important by a few who did not have support to quit and stay quit from others around them (‘*a mental boost’* or *‘invisible friend’*). The texts helped them to feel less alone, were a ‘*constant reminder*’, ‘*encouraging*’ and a ‘*positive reinforcement*’ which was helpful.

*“They’re great because they actually reinforce hey there’s someone looking out for you, you know and you need to do this and you need to do that, it’s like a positive reinforcement, it’s like somebody giving me a yeah you can do this, they come randomly, they come at whatever time, so it’s random out of the blue to say hey stay strong, keep going, so I think they’re great, especially as I said I was on my own and I thought of it as a positive reinforcement randomly sent to me, it’s excellent”* [Relapsed/NIC+S3P/3 Month FU/Female/56 years/Australia].

*“I think that [QuitCoach] together with the text messages was a good combination rather than one or the other, I think they went well together you know, I don’t think it would’ve been as effective just having one”* [Lapsed/S3P/6 Month FU/Female/35 years/Australia].

Some participants mentioned re-reading the study texts to remind themselves why they were quitting and to stay stopped, particularly during an urge. Others described taking screenshots or referring to the texts when struggling during an urge to remind themselves about their motivations for quitting, for example:

*“I think that every time I’ve wanted to smoke or had an urge to smoke I’ve just reminded myself why I quit, and I had a look back over the texts that had been sent to me, and I had a look back over those and they helped, it’s just reminding myself why I quit more than anything”* [Abstinent/NIC+S3P/3 Month FU/Male/24 years/England].

The tailored texts were described as ‘*thorough*’ and ‘*helpful and motivational’.* After coming off Champix and redoing an assessment, the times at which the tailored texts were received became ‘*more varied*’, ‘*unexpected*’ and ‘*random*’ which was a welcome change. Again, a few commented that it would be better if the tailored and interactive texts could focus less on products if they were not using them and focus on motivational messages. Specific references to a nicotine product the participant is not using could be due to a participant error when they were online, failure to notify the system of having stopped using a product, or a coding error. An illustration is provided in the example below; complaints such as this were rare as the system was programmed to only send relevant messages, based on participant preferences.

*“It texts me as if I am a vaper, if that makes sense, it texts me saying erm take a moment to think about how much better your life is since you quit smoking and started vaping and things like that but obviously I don’t vape, I think out of the whole time I’ve been using it I’ve only had about four texts that obviously include vaping”* [Abstinent/NIC+S3P/3 Month FU/Male/24 years/England].

Others mentioned the frequency of the texts could be increased and had ‘tailed off’ too early. For others, a few months of receiving the text messages was enough.

*“With the text messages they kind of tailed off too early, the frequency to begin with was really really great and really worked for me, but then the movement to greater frequency, I’m sure some people would find it annoying but it’s almost better to be an annoyance than having too few text messages and for someone to not have it at the right moment”* [Lapsed/NIC+S3P/3 Month FU/Male/29 years/England].

Others were more negative about the texts, similar to responses to text messages from the other arms of the trial. The messages frequently reminded them of smoking and triggered urges to smoke.

*“It makes me think of smoking when I’m not actually thinking about smoking”* [Abstinent/S3P/3 month FU/Male/69 years/Australia].

However, a few found that reminder of trying to quit smoking as beneficial. Again, the first text of the day was welcomed by some but annoying to others, even when it was acknowledged that the texts had helped with urges to smoke in the morning. Whilst helpful, receiving texts later in the day at other trigger points such as teatime and after dinner would have been appreciated.

“*Instead of throwing them all at the person first thing in the morning”* [Abstinent/NIC+S3P/3 Month FU/Female/50 years/England].

A few remarked that they no longer opened the text messages after a certain period of time.

*“After a while you know what they are so you don’t open them up anymore*” [Lapsed/NIC+S3P/3 Month FU/Male/24 years/Australia]

However, they appreciated receiving them as acknowledging that perhaps ‘subconsciously’ they were modifying their behaviour.

*“It just reminds you about cigarettes and stuff you know what I mean […] Yeah like I mean you’re not thinking about nothing and then all of a sudden you get a text message saying blah blah blah you know from the Quit Text and you think woah I wasn’t thinking about cigarettes and then you just made me”* [Abstinent/NIC+S3P/3 month FU/Female/51 years/England].

*“I wasn’t thinking about cigarettes and stuff like that, well they’d sent me the e-cigarette but I didn’t think about it, but every time I saw those text messages I thought about it, I don’t know why but in my normal routine I feel like those messages remind me of cigarettes”* [Lapsed/NIC+S3P/3 month FU/Female/39 years/England].

Some also felt that the constancy of the messages suggested that they were wanting them to slip up.

*“Have you had a fag and not told us and I’m thinking that is something that I don’t want to hear I’m trying to pack in smoking here, it seemed as if they were egging me into lapsing because it was the norm*…. *should I have a fag because they want me to lapse type thing”* [Abstinent/NIC+S3P/3 Month FU/Female/50 years/England].

Others reported not accessing the study website often as they had appreciated the texts more. For example, a participant remarked that they initially logged in to access QuitCoach out of ‘curiosity’ but did not use it because it reminded them of cigarettes and they did not want to be reminded, and the tailored text messages had been sufficient. There was a clear preference expressed by many for face-to-face contact rather than tailored text messages which some felt they would disregard more easily.

Suggestions for improvements to the tailored texts included more personalisation and one remarked that they would prefer a shift in terminology from ‘quitting smoking’ to ‘stopped smoking’ as ‘quitting’ sounds as if you are still doing it. Some remarked the frequency of the tailored texts had been too much, for example a participant commented that they were ‘*slightly irritated by my phone going all the time*’. Many wanted to be able to nominate how many texts they would receive. Another noted that the texts were:

*“just platitudes, they aren’t telling me anything that I didn’t know, they might be useful for some people but for me they really irritated me something stupid [laughs]* […] *to be honest all I can think about the messages is that they irritated me”* [Abstinent/NIC+S3P/3 Months/Female/48 years/England].

In addition, a participant stopped the texts before going on holiday due to perceiving (inaccurately) that there might be additional charges for receiving text messages abroad.

## (4) Battling to overcome craving

Craving was a key concern for most interviewees. When asked about when they started to become aware of urges, most frequently it was in the context of quitting. Indeed, one stated that they only really became aware of these when they stopped smoking, as usually urges were indulged. Many participants described how it felt to have urges or craving, for some having to be constantly on their toes:

*“Early on I would say I was getting quite a few, but yeah it was always quite reassuring, but it is a daily battle I guess, not so much now but earlier on it was an ongoing thing that you’d have to be on your toes and be aware of possible things that could be a trigger or erm yeah, without even knowing what’s a trigger for you”* [Lapsed/NIC+S3P/3 Month FU/Female/30 years/Australia].

Some would often describe a conversation in the brain as *‘a battle’* that played out in different ways. Although one participant said the voices changed to encouragement when trying not to relapse.

*“This constant sort of heckling in the brain about needing to satisfy particular sort of, yeah a particular craving for what you know is a cigarette, it’s not food it’s actually a cigarette”* [Relapsed/Usual Care/3 Month FU/Male/52 years/Australia].

*“Oh look I think a person you know has to be more strong-willed in their efforts to quit if you know what I mean, and not fall for the voice in the head[..] it seems that all of a sudden it has a grip on you. Craving gets really really strong sometimes it seems overpowering, you know, and you just buckle under pressure sometimes I think”* [Lapsed/NIC/6 Month FU/Male/28 years/Australia].

When asked how long urges to smoke lasted, answers varied from ‘a couple of minutes’ with another saying ‘a good ten minutes’. Participants described how sometimes they gave in to the urges, as they were completely overwhelming ‘*when I was dying for a, like actually dying for a smoke’* to the extent that they would *‘go down the street and bum one off someone’.* Sometimes participants differentiated among various types of urges *‘there’s so many different types of cravings and yeah urges to smoke’.* For example, one participant differentiated physical urges from emotional urges when they were going through a difficult time.

*“It was just a pressure building and I just couldn’t cope”* [Relapsed/NIC+S3P/6 Months, Female, 69 years/Australia].

*“It sort of like starts off as like a tightness in my chest type-thing, from there I’m like I need a smoke, my mind won’t stop thinking about it where it’s like erm obsessive thoughts about it almost and then if I can’t get it I get really agitated you know I get the tightness in the chest and things start happening”* [Relapsed/Usual Care/6 Month FU/Female/33 years/Australia].

*“The first wave I found it so easy, physical cravings were taken care of with patches and lozenges, I really really wanted to quit and still do, but yeah and it was really the second wave the cravings it was kind of sort of more emotional more than anything else”* [Relapsed/NIC+S3P/6 Months/Female/69 years/Australia].

*“So at that point I didn’t care about stopping any more, my sort of erm feeling of having almost like no resources was stronger than anything else at that time”* [Lapsed/NIC/3 Month FU/Female/57 years/Australia].

Some abstainers and lapsers reported that they were still getting urges, even after some time, but for others, that battle lessened over time.

*“I’m always feeling tempted to smoke”* [Lapsed/UC/3 Month FU/Female/38 years].

*“But yeah that went away over time and now it’s not even a thought that’s in my head like…. It’s totally gone”* [Lapsed/NIC+S3P/3 Month FU/Female/30 years/Australia].

## (5) Differential responses to lapses and relapse

There were differences between participants in terms of how they interpreted lapses to smoking. Also, regardless of how they interpreted lapses, frequently lapses and relapses were not defined as they are in academia, with a slip up (i.e. smoking even a few puffs of a cigarette) being referred to as a ‘relapse’.

For some abstainers, a lapse would be regarded as a failure and likely to progress to a full-blown return to smoking. Some suggested that *‘you’re either a smoker or not’* and therefore a lapse was the equivalent of relapse and there was no distinction between the two – lapsing was therefore to be avoided at all costs. In these instances, a lapse was grounds for having to start new quit attempt, for example:

*“I just keep telling myself a lot of the time that if I even have one cigarette I have to start again and that’s a very strong motivator for me”* [Abstinent/UC/3 Month FU/Female/39 years/Australia].

*“I know that if you have one puff that can just get you back in, [….] I would say the reason I’ve been more successful this time is because it happened to me before, that they sucked me back in”* [Abstinent/NIC/3 Month FU/Female/54 years/Australia].

*“The minute you have a ciggie it opens that up in your head and then once you’ve done that you’re just back to square one, so never having that first cigarette is the biggest thing and remember there’s no such thing as just one”* [Abstinent/NIC/3 Month FU/Male/54 years/England].

For these participants who believed a lapse was a personal failure, then the lapse could progress to relapse, for example:

*“I had a cigarette and I stopped again […] I had the temptation but I was like fighting with the temptation that I shouldn’t be smoking I shouldn’t be smoking, and I kept telling myself that, reminding myself, and then eventually I said one more won’t hurt me, and after a week I think I took another fag, and from there it was frequent”* [Relapsed/UC/6 Month FU/Male/50 years/England].

Sometimes the physiological response to a lapse meant that more cigarettes would follow. A few alluded to being ‘*gripped*’ by urges to smoke more after one puff, referring to it as a recurring ‘*cycle*’ that ‘*sucked you in*’ or was ‘*easy to fall back in to*’.

For others, there was a sense that learning the best strategies takes time and comes with experience ‘*slipping isn’t failing’*. Among many, a lapse was viewed as a transitional learning experience and for these participants the progression to relapse was less probable. Many reported how they were more likely to experiment with alternative coping strategies in the future, which may lead to the learning of more effective coping responses in high-risk situations. Indeed, for these participants, relapse prevention appeared to be an iterative process as they talked about learning from the situations and strategies used during past lapses to succeed. Abstainers, in particular, conceived of relapse as a dynamic process of learning strategies and techniques to cope with temptation and cravings over successive quit attempts, of expanding and honing their capabilities over time and making use of existing resources available to them to achieve this.

For these participants, a lapse was differentiated from relapse, or more specifically, a lapse or a slip was not a failure ‘*it’s not falling off the wagon’*, but rather an opportunity to experiment and learn about what is required for them, in their particular circumstances, to stay quit, for instance:

*“Relapse for me, it doesn’t mean that I’ve failed, it means that I’ve tried and I’ll have to try harder […] relapse prevention I think is about how to control my urges, it just makes me more confident if I manage to do it, so I also think it links to someone’s self-confidence, if you know what I mean, the more confident you are in thinking that you’ll achieve your goal they more successful you become”* [Abstinent/NIC/3 Month FU/Female/38 years].

*“Your success will probably be built on failures it doesn’t matter yeah [..] it’s just part of the process so actually it’s getting to know how your addiction works and getting to know how you overcome it [..] just go straight back to giving up”* [Abstinent/NIC/3 Month FU/Male/59 years/England].

For those who viewed a lapse as a learning experience, their successful coping was described as having been built on by learning from previous quit attempts. Lapses were positioned as part of the learning process to the extent that they help one know what to do in order to recover and return to abstinence, for example:

*“Don’t beat yourself up because you might’ve slipped up once in the week so what, don’t beat yourself up about it, if you slip up every day that’s a different thing, well that’s what I’m doing, I didn’t beat myself up about it, I didn’t go oh well I’ve blown it I’ve got back on it”* [Lapsed/NIC/3 Month FU/Female/60 years/Australia].

*“It’s just a setback, you haven’t failed, it’s just a setback and start again but you know what you’ve learnt in the last few months and just apply them again, you can do it, […] it’s easier to go back to ciggies than it is to stay stopped, I’d just say you know just try and do it again and keep on going, use these cigarette things where they help you and you’ll do it, eventually you’ll do it”* [Abstinent/NIC/3 Month FU/Male/54 years/England].

*“Keep persisting and if you fall off the band wagon just get back on again and [laughs] yeah it’s like that saying if you fall off the horse just get back on and try again. I mean it took me you know like three attempts just to finally stop”* [Abstinent/NIC+S3P/3 Month FU/Female/33 years/England].

Some participants described how they had learnt triggers to smoke or which situations to avoid or which attitude or approach was required through previous lapsing experiences, which enabled them to have more ‘control’ over urges to smoke, for example:

*“When I have done it in the past, it’s more about how I’ve approached, like if I go into it with oh it doesn’t really matter type-thing and I’m really blasé about it then I find I’m just like one more packet won’t hurt me, if I’m not strict with myself it turns back into full-blown relapse where I’m smoking all the time […] I find that I’m a lot more strict with myself, yeah if I go into it very blasé I find that I lose control”* [Relapsed/UC/6 Month FU/Female/33 years/Australia].

Many participants reported that lapses were particularly common in situations involving alcohol consumption. Alcohol and smoking were frequently described as going together, ‘*hand-in-hand*’ and several participants reported difficultly in refraining from smoking while consuming alcohol.

*“It’s mostly just the nights out when there’s alcohol involved that’s when I relapse”* [Lapsed/NIC+S3P/3 Month FU/Male/24 years/Australia].

There was some discussion of ‘permissive’ lapses 30. These were lapses that they decided to allow.

*“I’ve just thought that I’ll decide to have a smoke today”* [Lapsed/S3P/6 Month FU/Female/35 years/Australia].

Or they were lapses that participants felt were somehow under their control, ‘*I felt that it was my own decision and I was kind of empowered*’. Permissive lapses were described as ‘disappointing’, ‘upsetting’ and ‘annoying’, though had been ‘justifiable’ as some reported how they ‘still felt quite in control of that decision’ to smoke as they were not buying cigarettes, or not carrying cigarettes around all the time, and therefore did not consider themselves to be a smoker, as follows:

*“A little bit disappointed in myself I guess, but I still felt quite in control of that decision, so I guess I was able to justify to myself, you know like it’s OK I’ll just have one, and I wouldn’t consider myself to be a smoker again, I haven’t bought a packet of cigarettes, I don’t carry them with me all the time you know. It doesn’t matter if I just have one, because that’s not going to ruin my whole plan of quitting so I was still quite focussed on the end goal of not becoming a full-on smoker again”* [Lapsed/S3P/6 Month FU/Female/35 years/Australia].

Following the lapse, they would want to ‘*move on’* to go back to quitting. However, serial lapses were common among these participants. Alcohol was again frequently involved in the occurrence of these permissive lapses. Previous quit attempts had equipped participants with knowledge about how to cope with temptations to smoke while socialising and drinking alcohol, for example:

*“There were times when I hadn’t smoked for two years, and you just drop your guard, you say save me some of that cigarette, and the next minute you buy twenty then, so it’s the old adage isn’t it, if you’re socialising with alcohol, or even sometimes just socialising, it’s funny, you could be in a good mood or sometimes if something really goes wrong or you’ve had a bad day you know, I think if you’re not as strong as I am now, when I was weaker if something, if I got bad news, your first thought would be I need a cigarette, whereas now I know that if I buy a packet of cigarettes I’m not helping myself”* [Lapsed/NIC/3 Month FU/Male/44 years/England].

Despite determination to stay quit, it was apparent that some felt that a lack of support and negative affect, such as stress, loneliness or boredom, or unexpected life events (such as a relationship ending or loss of a loved one) contributed to lapses which in some cases were followed by prolonged periods of returning to smoking. Having been smokers for a long period of time contributed to this - smoking had been the response to such occasions over a period of time and unlearning this was difficult. However, there were also a few reports of lapse progressing to relapse while relaxed, on holiday for example, which for some had also been due to the low cost of cigarettes.

# Chapter 6: EMA Sub Study Results

Table 22 shows the characteristics of participants recruited to the EMA sub study. Around 53% of EMA participants were recruited from Australia. The sample comprised of largely middle-aged smokers and around half (52%) were female, 25% were in full time employment and 68% were in receipt of benefits. Recruitment varied across the conditions, with 46% of the target usual care participants enrolled, while only 28%, 40% and 44% of the target participants were enrolled from the S3P, NIC and NIC+S3P conditions, respectively.

Table 22. Baseline characteristics of EMA sub study participants

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Baseline characteristic** | **UC**  **(N = 23)** | **NIC**  **(N = 20)** | **S3P**  **(N = 14)** | **NIC+S3P (N=22)** |
| Age, years (median (IQR) | 47 (34-57) | 45 (33-53) | 45 (32-62) | 48 (31-56) |
| Female, N (%) | 13 (56.5) | 8 (40.0) | 4 (28.6) | 16 (72.7) |
| Partner smokes:  Yes, N (%) | 4 (17.4) | 0 (0) | 2 (14.3) | 5 (22.7) |
| Mental health condition: Yes, N (%) | 11 (47.8) | 6 (30.0) | 3 (21.4) | 8 (36.4) |
| In full time employment, N (%) | 6 (26.1) | 6 (30.0) | 4 (28.6) | 4 (18.2) |
| Receiving benefits, N (%) | 14 (60.9) | 15 (75.0) | 11 (78.6) | 14 (63.6) |
| Heaviness of Smoking Index, N (%)  Low  Medium  High | 5 (21.7)  15 (65.2)  3 (13.0) | 4 (20.0)  15 (75.0)  1 (5.0) | 1 (7.1)  11 (78.6)  2 (14.3) | 0 (0)  19 (86.4)  3 (13.6) |
| Using base medication, N (%) | 12 (52.2) | 9 (45.0) | 8 (57.1) | 14 (63.6) |
| Ethnicity (Australia, N = 42):  Australian born (non-aboriginal), N (%) | 11 (84.6) | 9 (75.0) | 5 (83.3) | 10 (90.9) |
| Ethnicity (ENG, N = 37):  White British, N (%) | 8 (80.0) | 8 (80.0) | 8 (100.0) | 8 (72.7) |
| Country, N (%)  AUS (n=42)  ENG (n=37) | 13 (56.5)  10 (43.5) | 12 (60.0)  8 (40.0) | 6 (42.9)  8 (57.1) | 11 (50.0)  11 (50.0) |

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Table 23 shows the smoking status of the EMA participants at the approximate time they were recruited into the sub study.

Table 23. Smoking status of participants when joining EMA sub study a

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Smoking status** | **UC**  **(N=23)** | **NIC (N=20)** | **S3P (N=13)b** | **NIC+S3P (N=22)** |
| Abstainer (not a puff since baseline survey), N (%) | 16 (69.6) | 12 (60.0) | 10 (77.0) | 17 (77.3) |
| Lapser (smoked, but not seven or more consecutive days since baseline survey) N (%) | 5 (21.7) | 8 (40) | 3 (23.0) | 5 (22.7) |
| Relapser (seven or more days of continuous smoking since baseline survey) N (%) | 2 (8.7) | 0 (0) | 0 (0) | 0 (0) |

a As reported at three month follow up survey

b Data is missing for one participant in the S3P arm

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

Participants were asked to report every lapse they experienced during monitoring in real-time. Overall, 54 participants reported a total of 227 lapse episodes during monitoring (average of 4.2 lapses per lapser); 68.4% of all the participants in the EMA sub study thus experienced one or more lapse episodes during the three weeks of monitoring). The number of lapse episodes across the four treatment groups was UC = 86; S3P = 62; NIC = 36; S3P + NIC = 43.

Among 78 participants (one EMA sub study participant had missing data; Table 23) classified as abstainers, lapsers and relapsers when joining the EMA study, 33 (60% of the participants initially categorised as abstainers), 18 (85.71% of lapsers) and 2 (100% of the relapsers) reported a lapse in real-time during the EMA monitoring.

Nine participants who joined the EMA sub study as ‘non-relapsers’ (N=76) experienced five or more lapses during the three-week monitoring period.

The antecedents and immediate consequences of lapse episodes, by treatment group, are shown in Table 24. Of the 227 smoking lapses reported in real-time by participants, 168 events (UC = 69 events; S3P = 51; NIC = 19; NIC+S3P = 29) included any contextual data and hence could be used to explore correlates of lapses. These lapses were reported by 39 of the 54 lapsers (UC = 12 lapsers; S3P = 5; NIC = 13; NIC+S3P = 9).

None of the intervention groups differed significantly from the usual care group in terms of the level of craving reported during lapses. As users of high-dose nicotine patch have been shown to be more likely to lapse under situations that involve low levels of craving 27, we examined the frequency of lapses that occurred in situations with little or no craving. Overall, approximately a third (32.7%) of lapses occurred in low craving situations (defined as events where craving was rated as <=10 on the single-item 0-100 craving measure). Surprisingly, participants in the S3P group were significantly more likely than those in the usual care group to report lapses during low craving intensity (66.9% vs 16.1%, p < .05); neither the NIC (25.7%) or the NIC+S3P (25.2%) groups differed from the usual care group. Participants in the intervention groups did not differ from those in the usual care group in levels of concentration immediately before a lapse episode (Table 24).

Previous studies have reported that the use of coping mechanisms during a cessation attempt is associated with better treatment outcomes. We examined the use of coping mechanism reported during lapse events. Overall, participants reported using coping mechanisms—either behavioural or cognitive—in less than a half (43.2%) of lapse events (UC = 51.3%; S3P = 23.1%; NIC = 51.5%; NIC+S3P = 34.4%).

Following a lapse, participants in the S3P group were significantly more likely to feel like abandoning their quit attempt compared to usual care participants (Table 24). Conversely, participants in the NIC+S3P group reported being significantly less likely to feel like abandoning their quit attempt compared to usual care participants.

Table 24. Characteristics of lapse episodes, by treatment group

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Lapse Episodes** | **UC**  **(N=69)** | **NIC (N=19)** | **S3P (N=51)** | **NIC+S3P (N=29)** |
| Mean (SD) number of lapses | 5.8 (12.00) | 1.5 (0.66) | 10.2 (18.41) | 3.2 (3.87) |
| Mean (SE) craving before lapse | 39.93 (6.95) | 44.59 (9.74) | 18.95 (8.41) | 56.52 (8.91) |
| Concentration a before lapse - Mean (SE) | 37.54 (6.69) | 29.64 (8.83) | 14.12 (8.21) | 30.20 (8.35) |
| Felt like abandoning quit attempt after lapse b - Mean (SE) | 59.04 (6.58) | 65.41 (8.92) | 97.60‡ (7.90) | 30.04‡ (7.91) |

*Note:* Analyses are based on the 168 lapse episodes with contextual information. Data are presented as modelled means or means of means (for lapse counts)

a Concentration was assessed as the mean of two items: “Last 15 mins: Hard to concentrate?” on a scale of 1-100, and “Last 15 mins: Difficult to think clearly” on a sliding scale of 1-100.

b Felt like abandoning quit attempt rated on a sliding scale of 1-100.

‡ Significantly different from usual care group.

UC: usual care arm, S3P: Structured Planning and Prompting Protocol arm, NIC: nicotine product arm, NIC+S3P: Nicotine product + S3P arm

# Chapter 7: Health economics

As described earlier, the health economics analysis could not be carried out as 12 month data was not collected in the curtailed trial. However, it is estimated that the development of the S3P intervention for the trial cost approximately £9000.

Although no 12 month data is available, the EQ5D was administered at baseline and the data are presented in Table 25, There was some variation in the dimension scores by arm, but subjective ratings of participants overall health at baseline (VAS scores) were similar and the majority of participants were in good health.

Table 25. EQ-5D visual analogue scale (VAS) score a and dimension responses b by arm

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **UC (N=60)** | **NIC (N=58)** | **S3P (N=57)** | **NIC+S3P (N=59)** |
| **VAS score, median (IQR)** | 69 (50-80) | 70 (65-80) | 70 (60-81) | 70 (58-84) |
| **Mobility, N (%)** |  |  |  |  |
| No Problems | 40 (66.7) | 44 (75.9) | 41 (71.9) | 44 (74.6) |
| Slight problems | 11 (18.3) | 9 (15.5) | 9 (15.8) | 5 (8.5) |
| Moderate problems | 4 (6.7) | 4 (6.9) | 4 (7.0) | 8 (13.6) |
| Severe problems | 5 (8.3) | 1 (1.7) | 3 (5.3) | 2 (3.4) |
| **Self-care, N (%)** |  |  |  |  |
| No Problems | 50 (83.3) | 53 (91.4) | 51 (89.5) | 55 (93.2) |
| Slight problems | 4 (6.7) | 4 (6.9) | 2 (3.5) | 2 (3.4) |
| Moderate problems | 5 (8.3) | 1 (1.7) | 3 (5.3) | 1 (1.7) |
| Severe problems | 1 (1.7) | 0 (0) | 2 (1.8) | 1 (1.7) |
| **Usual Activities, N (%)** |  |  |  |  |
| No Problems | 38 (63.3) | 40 (69.0) | 40 (70.2) | 48 (81.4) |
| Slight problems | 14 (23.3) | 13 (22.4) | 9 (15.8) | 5 (8.5) |
| Moderate problems | 2 (3.3) | 5 (8.6) | 2 (3.5) | 4 (6.8) |
| Severe problems | 3 (5.0) | 0 (0) | 6 (10.5) c | 2 (3.4) |
| **Pain/discomfort, N (%)** |  |  |  |  |
| No Problems | 27 (45.0) | 34 (58.6) | 28 (49.1) | 29 (49.2) |
| Slight problems | 14 (23.3) | 12 (20.7) | 15 (26.3) | 16 (27.1) |
| Moderate problems | 10 (16.7) | 10 (17.2) | 12 (21.1) | 11 (18.6) |
| Severe problems | 6 (10.0) | 2 (3.5) | 2 (3.5) | 2 (3.4) |
| Extreme pain/discomfort | 3 (5.0) | 0 (0) | 0 (0) | 1 (1.7) |
| **Anxiety/depression, N (%)** |  |  |  |  |
| No Problems | 23 (38.3) | 27 (46.6) | 26 (45.6) | 26 (44.1) |
| Slight problems | 15 (25.0) | 15 (25.9) | 18 (31.6) | 18 (30.5) |
| Moderate problems | 14 (23.3) | 12 (20.7) | 11 (19.3) | 9 (15.3) |
| Severe problems | 6 (10.0) | 3 (5.2) | 2 (3.5) | 4 (6.8) |
| Extremely anxious/depressed | 2 (3.3) | 1 (1.7) | 0 (0) | 2 (3.4) |

a The VAS is presented as a visual scale from 0-100 where 100 means the best health you can imagine and 0 means the worst health you can imagine. Particpants were instructed that ‘We would like to know how good or bad your health is TODAY’ and ‘Please mark an X on the scale to indicate how your health is TODAY.’

b For the dimension questions, participants were asked ‘Under each heading, please tick the ONE box that best describes your health TODAY.’

c Five participants report severe problems while one reports being unable to do usual activities

# Chapter 8: Discussion

The curtailed trial lacked power to detect effects that the interventions could reasonably be expected to have, but it nevertheless generated outcome data that can contribute to future meta-analyses, as well as novel data on ex-smokers’ reactions to different relapse prevention interventions.

**Acceptability of the interventions**

Initiation of allocated interventions was high, suggesting that both interventions are acceptable to recent ex-smokers. The qualitative study suggests that both interventions were perceived as sensible and helpful. Both interventions also obtained generally positive ratings. These are encouraging findings although, as noted below, need to be taken into account with the findings that NRT/e-cigarettes were more likely to be used than QuitCoach which most people used only once. Some relapse prevention interventions examined in the past seem to have generated little enthusiasm and there was a concern that smokers who have recently quit smoking may feel that they have achieved their objective and have little interest in trying to prevent any theoretical lapses. The positive ratings could have been in part due to the fact that some of the study participants were still in the early stages of smoking cessation rather than abstinent for at least four weeks, as originally planned. This, however, concerns only a minority of participants in Australia , and treatment ratings were positive at both trial sites. Overall, we can conclude most participants found their allocated intervention of some utility, but there was variation.

**Nicotine products**

Regarding nicotine products, e-cigarettes were selected more often than NRT in Australia (71% vs 29%), but the difference was not significant in England (54% vs 46%). This was unexpected in the English site, because e-cigarettes are more popular among UK smokers than NRT 13 14. Given that nicotine-containing e-cigarettes are banned from general sale in Australia, we expected they would be a popular choice there as this study provided a way to access these products. It is possible that smokers in England who attend stop smoking services are less likely to be interested in vaping, or that they were more affected by media scares concerning e-cigarettes than smokers in Australia where there is no vaping and so media scares may be less prominent. Nevertheless, concerns around the safety of vaping were more likely to be voiced by participants in Australia in the qualitative research.

The intervention consisted of recommending opportunistic use when at risk of relapse, but to use as much as need to prevent a return to smoking. At three month follow-up we found 53% of participants used their products at least occasionally (31% daily) and 40% at six months (23% daily). Of those still using their study product at least occasionally, 74% were using e-cigarette and 26% were using NRT at three months and 76% and 23% at six months (one person used both). This shows a higher extended use of e-cigarettes compared to NRT, but by a smaller margin than noted in a recent randomised trial 16. That trial, however, included nicotine patches as opposed to fast-acting NRT that was used here. Faster-acting NRT products generate higher rates of extended use than nicotine patches 31 32.

Regarding product safety, there were no SAEs related to trial medications. The most common AE reported was weight gain, which is a common side effect of quitting smoking 33. Indeed, it is notable that among all AEs, those in the groups provided with nicotine products were less likely to report them, suggesting a proportion of AEs are due to abstinence from nicotine. However, as the differences were not significant, this possibility should be treated with caution.

**Behavioural interventions**

Behavioural interventions included a series of practical recommendations for implementing behavioural and cognitive coping strategies imparted via the online QuitCoach and Problem Planner. The intervention was further accompanied by an intensive texting schedule that was tailored to participants’ responses to an online assessment and included an option for interactive messaging.

Although the comprehensive package received overall positive ratings, both for the online and the text-messaging components, its utilisation in terms of site visits, assessments and use of interactive texting was low. Most participants completed only a single QuitCoach assessment, typically immediately after joining the study (i.e. on the same website visit), and only a third reported using the Problem Planner. Only one participant used the interactive feature of the text messaging, indicating that participants either did not see a need for it, or were not aware of it. Future work may need to focus on encouraging reengagement with such tools. Most participants indicated that they only read the advice that the programme generated for them ‘quickly'. The qualitative study offers some insights into the reasons for this. Clients needed usernames and passwords to visit the site which represented a significant barrier to some of them; and the extensive text and long questionnaires may have also limited engagement with the programme. Some of these features were due to the trial components, but future iterations of the programme may look at simplifying access to the information as well looking at ways to present the content differently. The revised version of QuitCoach that was being programmed for the study (but ultimately not delivered by our IT consultants) would have provided the capacity to break the assessment and advice into smaller chunks. Use of a version with capacity to break the advice up and provide summary versions, as well as the full advice, may better meet the varying needs of participants.

We hoped that the detailed follow-up questionnaires would identify coping strategies that the behavioural intervention imparted (strategies used by S3P and NIC+S3P study arms but not in the other two arms) and highlight advice that was most popular, suggesting components that were particularly practicable and useful. Of the six listed strategies, five were used by the majority of participants at both three and six-month follow-ups. The most popular was reminding oneself of reasons for quitting, used by some 90% of participants. Some 80% used distraction. The most demanding feature that was the focus of the intervention, putting in place a pre-prepared plan for resisting temptations, was used by about a third of clients. However, unexpectedly, the proportion of those who reported using each coping strategy when tempted to smoke was practically identical in the non-S3P groups (UC and NIC only). This included the use of a pre-prepared plan. More relevant than whether planning occurred, however, may be the quality of planning - something which is more difficult to quantify. Recognising that most ex-smokers engage in some form of planning 34, the intention of the S3P intervention was primarily to increase the quality of existing planning strategies and to help ensure that they were remembered and acted upon at times they were needed. At the intermediate (i.e. three and six month) follow-ups, we could not ask participants in all study arms about whether they had formed strategies in terms of ‘if-then’ plans (implementation intentions). This would have made little sense to those in the non-S3P arms, but more importantly risk exposing these participants to a key idea underlying the S3P intervention. The EMA sub study also found no differences in coping strategies used by different study arms when faced with lapse situations. Overall these findings could suggest that the S3P intervention had limited effects on the actual behavioural responses to temptations to smoke. However, given the trend for this intervention to reduce relapse, it may have supported people in another way (e.g. promoting recovery from a lapse) that we have not investigated in this report.

**Process of relapse**

Only about half of the participants maintained sustained abstinence at six months. Of those taking part in the EMA sub study which monitored lapses in real time, two thirds experienced a lapse during the three weeks of monitoring. This included lapses in participants who were classified as having lapsed or relapsed already (N=20), but also 33 participants who were until the EMA monitoring classified as sustained abstainers. A good proportion of lapses happened when craving levels were relatively low; and many lapses made participants feel like abandoning their quit attempt. There was no clear signal of any intervention effects on these variables.

The EMA sub study found few significant differences between the usual care and intervention groups. A significant difference was observed in the experience of low-craving lapses. As noted earlier, it has previously been reported that users of high-dose nicotine patch are more likely to lapse under situations that involve low levels of craving 27. Here, however, participants in the S3P group were significantly more likely than those in the usual care group to report lapses during low craving intensity. This finding is difficult to explain, as participants in the S3P group were provided additional information about coping with craving and avoiding lapses, including the use of implementation intentions. However, it may be that those allocated to S3P were more likely to recover from a lapse, which is also something the content focuses on. This and other differences between groups need to be explored in future using more adequately powered studies before firm conclusions can be drawn.

**Some lessons from the trial tribulations**

The trial faced serious difficulties in integrating a proprietary online programme with the data collection requirements of a randomised controlled trial, which led to significant delays in recruitment. Future trials using such interventions need to consider the vulnerability of specific programmes and apps to the demands of data management. Even more importantly, trials that involve international collaborations need to research relevant data protection and IT security requirements as these can generate major hurdles.

Another issue that can serve as a warning to future projects were difficulties in recruitment. Recruiting recent quitters from quitlines proved much more challenging than expected, and we expected it to be hard. The main problems included: 1) marked drop-offs in the use of quitline services before recruitment; 2) reluctance to enrol in a new intervention study after succeeding with support already provided; 3) unwillingness to participate in a trial where they could be assigned to a pharmacotherapy intervention; and 4) greater difficulties experienced by quitline specialists to contact callers on their last scheduled call. In England, over the past few years, the throughput of the stop smoking services shrunk by over 60% from their inception and the services were relocated from NHS to local councils who commission private providers to deliver stop smoking treatments. The reorganisation and the change of service focus meant that only a few services remained that could contribute to research. Future studies, at least those conducted in England, that involve smoking cessation may need to identify recruitment venues other than stop smoking services. Planning for recruitment in other UK countries may have also been a useful strategy. However, this planning needs to take place early as gaining regulatory approvals takes time.

In Australia, we attempted to recruit other quitlines, but were unsuccessful, largely as a result of one am of the study involving vaping products. However, even if we had been able to recruit all quitlines, recruitment would have still been below what we needed. In Australia, we conclude that the required strategy of recruiting ex-smokers after successfully quitting for one month is not feasible, at least from services that had already provided a quite intensive program of help.

In Australia, we tested two alternative methods of recruitment: use of social media and recruiting from hospitals where patients are not allowed to smoke as inpatients. Our conclusion is that social media is likely a useful recruitment source, but use is complicated where there are complex inclusion criteria for the trial as there was in our case. Further, it is not likely to be a major approach for service delivery, although promoting effective programs on social media is likely to draw some traffic and may be able to do this at a reasonable cost.

With regards to recruiting from hospital inpatients, overall, initial recruitment there relied heavily on manual screening processes of patients’ smoking status and receiving referrals from other health professionals within the hospital. This process was later made more automated, but is something to consider early on in the set up process.

Common to both countries was a greater than expected intention to use medications or vaping devices for extended periods (more than three months) thus rendering them ineligible for this trial.

These issues highlight the need for pilot phases within large trials with clear stop/go criteria.

**Study limitations**

The key study limitation is the curtailed sample size that limited the power that the trial had to detect intervention effects. Study outcomes can still contribute to future meta-analyses. Related to study curtailment, the follow-up period was shortened from 12 to six months. As the efficacy of smoking cessation interventions typically declines over time, the hint we detected that the single interventions may show some efficacy needs to be interpreted with caution. Another consequence of the trial curtailment is the lack of biochemical validation. This means that the abstinence rates are likely to have been overestimated overall, and in particular in the intervention groups that received more input and may have felt a stronger obligation to report success. It is reassuring that the NIC+S3P group reported somewhat higher relapse than the NIC and S3P groups, but the numerical advantage of all intervention groups compared to usual care could still reflect different response expectations.

The trial curtailment also meant that the planned health economics analyses could not be carried out, as follow up data collection for the EQ5D and health service use questionnaire were only planned at 12 months.

The trial was originally designed to test the interventions following formal stop smoking treatment from either the English stop smoking services or Australian quitlines. The addition of recruitment via Facebook, St Vincent’s Hospital and Stoptober meant that 34% of participants had not received any formal stop smoking support. Furthermore, extending the eligibility window meant that some participants entered the trial after only one week quit in Australia, whereas others joined after three months quit. This variation reduces the focus on relapse happening from around one month as original planned. However, the notion that relapse prevention only begins at four weeks of abstinence is arbitrary. It can be argued that from the moment that a person stops smoking they require strategies that help prevent them from relapsing to smoking.

Another feature of the trial warrants additional caution in assessing relapse rates overall, in particular the interpretation of findings for the control group. The qualitative and EMA sub studies were originally planned to involve only a small sub-sample of a large trial, with identical sampling across study arms. In the curtailed study, the qualitative aspects of the project are relatively more important. A much larger proportion of the sample took part in qualitative interviews, approximately 40%, and about a third of participants took part in the EMA study. We were also unable to balance the proportions of lapsers, relapsers and abstainers within or between the study arms, and those participating in these sub studies were less likely to have relapsed compared with those who did not. A potential issue that this created is that qualitative interviews suggested that EMA data collection represented a perceived intervention, and the interviews themselves could have had this impact too. The EMA study and qualitative interviews could have provided not only motivational input, perhaps more memorable than online instructions because of their interactive nature, but could even impart or reinforce coping strategies via focusing on their details during surveys and EMA monitoring. Such input could, in theory, contribute to the lack of differences in the use of coping strategies between study arms discussed above. It could have also boosted abstinence rates, especially in the control group, and thus dilute any intervention effects. However given the self-selection for these sub studies it is not possible to make any definitive conclusions regarding these effects.

The overall six month follow-up rate was 88.5%, which is relatively high for trials of this type. Achieving higher follow-up rates is difficult as smokers who are unsuccessful tend to feel embarrassed and avoid contact. It is reassuring that follow-up rates across the four study arms were similar, as were the follow-up rates in the two countries. Nevertheless, incomplete data represents a limitation.

**Generalisability**

The majority of participants (66%) received structured stop smoking support before joining the trial. As such, the results may not be generalisable to populations who quit unaided, or without formal support. This is particularly true of the nicotine product arms, since e-cigarettes are readily available in England and are widely used without any structured support as an effective tool to quit smoking 35 36.

**Recommendations for research**

Efficacy of fast-acting nicotine products provided for use in emergencies and accompanied by text reminders for relapse prevention may deserve further exploration. Online training programmes have good intuitive validity and should be also further examined. An intermediate aim could be to develop delivery modes that ensure that participants recall the advice and act on it. Once this has been established, evaluating the intervention in a simplified package, e.g. as a mobile phone app, would be the natural next step. Another recommendation is that future trials should aim to initiate relapse prevention interventions around time of quitting. Delaying the offer until later in a successful quit attempt risks a reduced likelihood of treatment uptake. That said, it should also be available for those who have quit and seek extra help as well, but this is likely to represent only a minority, largely self-quitters who find themselves in trouble. There may also be utility in testing these interventions in those who are hospitalised and unable to smoke. Our experience suggests this will be best done if the relapse prevention interventions can be initiated while hospitalised so advice and/or meds can be provided before the person is discharged. Future studies should also consider using simpler designs, and plan for the challenges faced when integrating trial data management systems into existing programmes or apps. Furthermore, international collaborations involving such systems will need to factor in data protection and IT security requirements.

## **Conclusion**

Both interventions were well received and safe. The effects of the combined interventions did not surpass those of each intervention alone. There was a trend in favour of single interventions reducing relapse, but it did not reach statistical significance and there are reasons to interpret the trend with caution.

The EMA study showed two thirds of participants experienced a lapse, and around a third of these lapses happened when craving levels were relatively low. For many, lapses made participants feel like abandoning their quit attempt.

Adherence to nicotine products was high, with e-cigarettes preferred to medicinal nicotine products. Behavioural advice was appreciated but did not seem to affect behaviour. Nonetheless, the findings of this curtailed trial suggest that these interventions may have promise, but more likely as alternatives as there is no evidence they work additively or synergistically.

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# Contributions of authors

Professor Hayden McRobbie (Professor in Public Health Interventions) led on the original grant application, co-designed the trial, co-wrote the statistical analysis plan, trained staff, interpreted the study findings and co-led on the drafting of the report.

Mrs Anna Phillips-Waller (Research Manager) managed the English trial site, co-wrote the statistical analysis plan, trained staff, contributed to data collection, interpreted the study findings and co-led on the drafting of the report.

Dr Catherine El Zerbi (Postdoctoral Research Associate) conducted the qualitative interviews, co-wrote the statistical analysis plan, interpreted the study findings and assisted with the drafting of the report.

Professor Ann McNeill (Professor of Tobacco Addiction) led the qualitative sub study, co-wrote the statistical analysis plan, interpreted the study findings and assisted with the drafting of the report.

Professor Peter Hajek (Professor of Clinical Psychology) contributed to trial design, co-wrote the statistical analysis plan, interpreted the study findings and co-led on the drafting of the report.

Dr Francesca Pesola (Research Fellow) co-wrote the statistical analysis plan, analysed the study data and assisted with the drafting of the report.

Dr James Balmford (Research Fellow) assisted with the development, refinement and maintenance of the S3P intervention and electronic data management system, co-wrote the statistical analysis plan, interpreted the study findings and assisted with the drafting of the report.

Dr Stuart Ferguson (Associate Professor) led the EMA sub study, co-wrote the statistical analysis plan, interpreted the study findings and assisted with the drafting of the report.

Dr Lin Li (Postdoctoral Research Fellow) managed the Australian trial site, co-wrote the statistical analysis plan, trained staff, contributed to data collection, interpreted the study findings and assisted with the drafting of the report.

Professor Sarah Lewis (Professor of Medical Statistics) co-wrote the statistical analysis plan, provided statistical oversight and assisted with the drafting of the report.

Dr Ryan Courtney (Senior Research Fellow) co-wrote the statistical analysis plan, interpreted the study findings and assisted with the drafting of the report.

Dr Coral Gartner (Associate Professor) assisted with the study set-up in Australia, interpreted the study findings and assisted with the drafting of the report.

Professor Linda Bauld (Bruce and John Usher Professor of Public Health) assisted with the drafting of the report.

Professor Ron Borland (Professor of Psychology – Health Behaviour) led the Australian study site, co-wrote the original grant application, co-designed the trial, co-wrote the statistical analysis plan, trained staff, interpreted the study findings and assisted with the drafting of the report.

# Trial registration

This trial was registered on the ISRCTN registry (ISRCTN 11111428).

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# Protocol

The English study protocol is available at: <https://www.journalslibrary.nihr.ac.uk/programmes/hta/1315505/#/>

# Data sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to anonymised data may be granted following review.

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# Appendix 1 - Supplementary Tables

Table 26. Summary of protocol amendments in England

|  |  |  |
| --- | --- | --- |
| **Approved version a** | **Date** | **Summary** |
| 3.0 | 02/09/2016 | Original approved version. |
| 4.0 | 09/02/2017 | Clarification and rephrasing of sections, minor changes to simplify trial procedures, correction of minor errors, and changes to web application and data management processes as a result of the issues experienced with QuitCoach. |
| 4.1 | 08/08/2018 | Updated sponsor representative contact and addition of Stoptober campaign for participant recruitment |

a Versions 1.0 and 2.0 were drafts prior to ethical approval.

Table 27. Summary of protocol amendments in Australia

|  |  |  |
| --- | --- | --- |
| **Approved version** | **Date of approval** | **Summary** |
| 17-9-10 version | 15 Aug 2016 | 1st approved version by CCV HREC |
| 17-10-2 version | 11 October 2017 | Amendment to widen the eligibility window for participating to 7-100 days quit, and to post ads in social media to supplement recruitment through Quitlines. |
| 18-4-17 version | 6 Aug 2018  (HREC/18/SVHM/155) | Seeking approval to recruit participants from St Vincent’s Hospital, Melbourne. |
| 19-M-7 version | 5-6-2019 | Amendment proposal to reduce the study follow-up duration to six months and adjust reimbursement accordingly. |

Table 28. Trial committee members

|  |  |  |
| --- | --- | --- |
| **Name** | **Role** | **Committee** |
| Dr Nicola Lindson | Chair (independent) | TSC |
| Professor Marcus Munafò | Member (independent) | TSC |
| Ms Jo Locker | Member (independent) | TSC |
| Mr Dan Griffin | Public member (independent) | TSC |
| Dr Sue Cooper | Member (independent) | TSC |
| Ms Jamie Hartman-Boyce | Chair (independent) | DMEC |
| Dr Lynne Dawkins | Member (independent) | DMEC |
| Dr Margaret MacDougall | Member (independent) | DMEC |
| Mrs Anna Phillips-Waller | England Study Manager | TMG |
| Professor Hayden McRobbie | England Co-Investigator | TMG |
| Professor Peter Hajek | England CI | TMG |
| Professor Ann McNeill | England Co-Investigator | TMG |
| Professor Sarah Lewis | Senior Study Statistician | TMG |
| Mr Benoit Aigret | Head of Barts CTU (now King’s CTU) | TMG |
| Professor Ron Borland | Australia CI | TMG |
| Dr Lin Li | Australia Study Manager | TMG |

# Appendix 2 - Topic Guide

Qualitative sub study semi-structured interview questions

*Questions will differ depending on smoking/abstinence status, intervention condition and country. Below is a comprehensive list of the questions which will be tailored according to the above criteria. Probes will be used throughout to elicit maximum information. We will have access to baseline and follow-up data on smoking history, lapses, relapses etc. for the* ***purposes of reference only****.*

* Preamble on format and approx. length of time (45 minutes max)
* Emphasise confidentiality
* Emphasise that there are no right or wrong answers
* Warm up conversation and testing sound on audio recorder, with a question: How is it going? (Based on the response to this question, we will re-allocate to lapse/relapse/abstainer)
* Below, the questions marked with\* means refer to the intervention questions for appropriate arm of the study
* Clarify when last cigarette was, including just a puff of a cigarette?

**Take notes and return to unanswered and unclear responses at the end of interview**

**Questions for Lapsers** (adapted in line with any responses to the warm up)

* **Lapsers - *a puff in the last 2 weeks but not smoked daily for 7 or more consecutive days, including participants who have been serial lapsers***
* Have you had any cigarettes since [see REDCap for recruitment date], including just a puff of a cigarette?
* Can you tell me about any cigarettes that you have smoked in the last couple of weeks? First, when did you last smoke? How many and how often in last 2 weeks? Did you have just a few puffs or the whole cigarette? [*If relapse - switch, if abstinent – switch*] If multiple: was this one period of smoking or were they separated by cigarettes resisted? Now thinking about the first cigarette (in the last bout of smoking): What triggered that cigarette?
* Did you do anything to try to resist? If yes, what?
* Had you been in a similar situation before and successfully resisted?
* If yes: What was different this time?
* How many cigarettes did you smoke before you recovered and resumed abstinence?
* What did you do to resume your quit attempt? What thoughts did you have?
* Had you tried previously to resume abstinence? How did it go?
* Explore relationship to use of interventions below as appropriate\*.
* Explore relationship between intervention and identified triggers/situations as appropriate\*.
* How did you feel after smoking it? *[Relate to intervention questions below as appropriate]*
* Have you smoked any further cigarettes since that lapse? Can you remember the interval between your first lapse and second?
* Have you been supported or influenced by family members, friends and other smokers to quit smoking?
* Have you felt tempted to smoke further cigarettes since then? What strategies have you used to stop yourself smoking? *[Relate to intervention questions below as appropriate\*]*
* How has this lapse experience differed from any previous quit attempts and lapses, why different if so?

**Lapse Situations:**

1. Was there anything you could’ve done differently?
2. Did you anticipate that you might lapse in advance?

**Permissive Lapsing:**

1. How confident were you that you’d be able to recover from that lapse?
2. Which, to you, is the most important benefit of quitting?
3. Looking back, hopefully it will help other people, but can you recall the occasion of your first lapse, and then what happened the second time? Did you know you’d be become a smoker again?

**Questions for Relapsers** (adapted in line with any responses to the warm up)

* **Relapsers - *smoking daily for at least 7 consecutive days, including participants who were lapsing and then relapsed subsequently, as well as participants who were abstinent and then relapsed***
* Have you had any cigarettes since [see REDCap for recruitment date], including just a puff of a cigarette?
* When was the last time you smoked? [within 2 weeks]
* When did you first lapse? Can you say a bit about what you think might have led to this situation? Explore the situation leading up to the relapse, was it a lapse initially or a full-blown relapse in one go? *[Use questions above as appropriate if initially lapses (particularly in relation to triggers, interval between lapses, and between lapses and relapse, plus any differences with previous quit attempts and full-blown relapses)*
* Could you talk a little bit about resuming smoking, and how you feel about this? Have you previously tried to remain abstinent from smoking, and how do you feel about not being able to remain abstinent? *[Explore timing of relapse in relation to use of interventions\*]*
* Prior to the relapse had you been using any effective coping strategies, for example when you had an urge for a cigarette? Had you been using any coping strategies, and if yes, which strategy did you find to be most effective? Why did you think this strategy was particularly helpful? Were there any strategies you found to be ineffective, and if yes, could you say why you think this strategy failed? *[Relate to intervention questions below as appropriate\*]*
* What, if anything, might have prevented you from relapsing? *[Relate to intervention questions below as appropriate\*]*
* How confident were you feeling about staying stopped in the run up to your relapse?
* Have you been supported or influenced by family members, friends and other smokers to quit smoking?
* Will you be trying to quit again soon? *[Explore interest in using the interventions if so – explore if this is different to previous relapses, why different if so?]*
* How did you feel before relapsing? And now?
* How do you think you’d feel if you successfully quit smoking?

**Questions for Abstainers** (adapted in line with any responses to the warm up)

* **Abstainers - *previously lapsed, or indeed relapsed, but subsequently abstinent in the last week***
* **Abstinence at 12 months *- not a single puff in the last month at 12 month follow-up***
* **Continuous Abstinence *- not smoking a puff at each follow-up at 12 months***
* Just to check – have you smoked any cigarettes at all since the start of our study?
* What do you think lies behind your success on this quit attempt, and why? What are the main strategies/methods you have been using to help you stay quit? When did you start using the strategy/method?
* How often, if at all, have you had to make special efforts to resist smoking? Have you been supported or influenced by family members, friends and other smokers to quit smoking?
* Which, if any, strategies did you adopt? And which did you find to be the most successful?
* Explore use of interventions as below\*. *[Probe individual strategies and relate to intervention questions below as appropriate]*
* How do you feel since quitting smoking?

**\*Specific questions on Interventions specific to the 3-month follow-up**

*[Use knowledge of follow up data to explore answers]*

**All (including usual care)**

* Check length of time using base medications (from follow-up data) Need to know if they were using at time of lapse? If using any FAN, did you use any to try to control the urge?
* Can you recall receiving text messages? *[Check follow-up data for the one-week call to see if participant received and found useful the interactive texts. If available, skip]*
* View on messages, e.g. which types of messages were most helpful and why? Frequency of messages ok? [*Probe milestone reinforcers, motivational messages, hints etc.]*
* Suggestions for improvements
* Did you use any other products to help you stop smoking since xx date? If yes, explore why, what, how frequently, appeal etc. [Specific questions for specific products e.g. EC/NRT]

**S3P**

* How often did you use the QuitCoach program and for how long? Overall how useful was this and what did you find useful? Explore when/why they accessed it, frequency etc., which aspects used?
* How easy did you find it to complete the web-based assessment?
* What do you remember about the tailored advice you were given about staying stopped? Did you find it to be helpful/relevant on every occasion? How could it be improved?
* Do you recall the structured tool that helped you to generate statements about strategies that you could use when the urge or temptation to smoke occurred? Did you generate any such statements? Did you use your strategies? How could this tool be improved?
* How useful did you find the follow-up call about how to use the S3P materials? How could it be improved? *[Only for participants who were contactable for follow-up call]*
* Check self-reported frequency of accessing the S3P online.
* Link usage to lapse/relapse timing and whether still using and why?
* Further suggestions for improvements

Nicotine products

* Check data about product chosen - I believe that you chose [see REDCap for EC/NRT product], is this correct?
* Why did you choose this product? Probe, e.g. had you used this product before? (or a similar product)?
* What is your overall impression of it?
* [For current use of product check REDCap follow-up data] How is it helping you?
* Do you enjoy using it, or do you find it a chore?
* Are there any aspects of use you don’t like?
* How often did you use the smoking replacement product and for long? Did you find it to be helpful/relevant on every occasion? Overall how useful did you find it and why?
* What do you recall of the materials we provided explaining how to use the product?
* *[Check follow-up data for the one-week call to see if participant received and found useful the interactive texts. If available, skip*] Did products arrive on time, ok etc.?
* Did you use the product at all after receiving it? Probe frequency/quantity/any difficulties using it/appeal?
* [*Only for participants who were contactable for follow-up call – see REDCap*] How useful did you find the follow-up call about how to use the smoking replacement product? How could it be improved?
* How do you access the product if still using?
* For lapsers and relapsers: were you using the product when you lapsed/relapsed?
* Did you continue to use it after the lapse/relapse? If you did not use it again, why not?
* Are you still using now?
* Suggestions for improvement e.g. would it have been helpful to have been provided with free products for longer?

**S3P plus Nicotine products (combine questions above)**

* To what extent, if any, do you think combining these two strategies worked well in helping to quit smoking? If you think they worked well together, could you say how? If you think the combination didn’t work well, could you describe why?

**E-Cigarettes:**

1. What do you understand about the relevant risk between smoking and nicotine?
2. Why are you tapering the nicotine (if relevant)?

**Final questions**

* Do you have any thoughts as to how we could improve our materials/product selection/provision etc.? When, by whom, where etc.? If favourable, do you think our intervention should be given to all those who have stopped smoking after using the SSS or Quitline?
* Do you think getting this help at around 1 month quit was a good time, or would you have liked it at around the time you stopped?
* Strategies around confrontation and avoidance of situations identified by participants as high-risk? Ask what their views are.
* Confidence about staying quit in the future, and perceived barriers to staying quit.

# Appendix 3 - Example coding frame for ‘Lapses’

**Definitions**

Slip up

Serial lapses

Full-blown relapse

Permissive lapses

Anticipating lapses

**Context**

Settings

Stress

Loneliness

Boredom

Alcohol

Adverse situations

**Interpretations**

Failure due to own ability

Failure due to context

Learning experiences

Unlearning previous patterns

A test of resolve

Confidence

Shame and guilt

**Responses**

Physiological sensations

Recovering and resuming

Learned techniques for coping with cravings

Persistence

Relapse